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Review Article

Retinoblastoma : Recognise the Disease early and save a child's life

Swathi Kaliki

Abstract : Retinoblastoma is the most common malignant intraocular tumor of childhood, with an incidence of 1 in 16,000 to 18,000 live births. The most common symptoms of retinoblastoma are leukocoria and strabismus. The diagnosis of retinoblastoma is delayed in the developing countries when compared to that of developed countries. The management of retinoblastoma has dramatically changed over the years from previous radiotherapy methods to current chemotherapy strategies. The treatment of choice in less advanced cases is chemotherapy and in more advanced cases is enucleation. With the improved treatment strategies, patient survival, globe salvage, and vision salvage in patients with retinoblastoma has drastically improved over the years. The aim of this article is to discuss the presenting features, treatment strategies, and prognosis of retinoblastoma.

Key Words : Eye Tumor, Retinoblastoma, Radiotherapy, Chemotherapy, Enucleation

Introduction

Retinoblastoma is the most common malignant intraocular tumor of childhood. James Wardrop first described it as a clinical entity in 1809, and Verhoeff proposed the term retinoblastoma in 1922, which was adopted by the American Ophthalmological Society in 1926[1,2].

Incidence of retinoblastoma

The incidence of retinoblastoma is 1 in 16,000 to 1 in 18,000 live births[3,4]. It represents 11% of cancers developing in the first year of life, and 3% of the cancers developing among children younger than 15 years[5]. It is estimated that, worldwide, 7202 to 8102 new cases are detected each year, of which 5819 to 6545 cases (81% cases) are from Africa and Asia[6].

Pathogenesis of retinoblastoma

Retinoblastoma is a hereditary malignancy with approximately 40% cases having an inherited form of disease caused by heterozygous germline mutation in the RB gene (RB1). Knudson proposed the "two-hit hypothesis" to explain the pathogenesis of retinoblastoma.[7] Ten percent of patients have familial retinoblastoma, who inherit RB1 mutation from a genetically affected parent. In such cases, every cell in the body of affected children contains a germline RB1 mutation (the first hit). Mutation of the remaining RB1 gene copy in a retinal cell (the second hit) causes retinoblastoma.[8] In another 30% of children with sporadic hereditable retinoblastoma, the germline RB1 mutation occurs as a de novo genetic event and their parents are genetically normal[9]. The remaining 60% children have sporadic nonheritable retinoblastoma, in which the tumors occur due to two somatic RB1 mutations in a single retinal progenitor or precursor cell. Based on the hereditary and inheritance pattern, retinoblastoma is classified as somatic or germline, sporadic or familial, and nonheritable and heritable.

Signs and symptoms

Retinoblastoma is usually diagnosed between the ages of 3 months to 3 years, with 95% of cases diagnosed before the age of 5 years[10, 11]. In rare instances, the tumor can be detected at birth or in adulthood. The tumor can be unilateral or bilateral. Overall, the mean age at presentation of retinoblastoma is 18 months. The mean age at presentation of unilateral cases is 24 months and for bilateral cases is 12 months[10,11].

The most common presenting complaint in children with retinoblastoma is leukocoria or a white pupillary reflex (60% to 70% cases). The second most common complaint is strabismus (20% to 25% cases).[11,12] The other less common presenting features include pseudohypopyon, hyphema, heterochromia iridis, unilateral mydriasis, red painful eye, proptosis, and orbital cellulitis (Figure 1). However, in contrast to the reports from the developed countries, the reports from some of the developing countries suggest proptosis as the most common presenting feature of retinoblastoma (55% to 85%), indicating a delayed diagnosis of the disease in the developing world[13,14].

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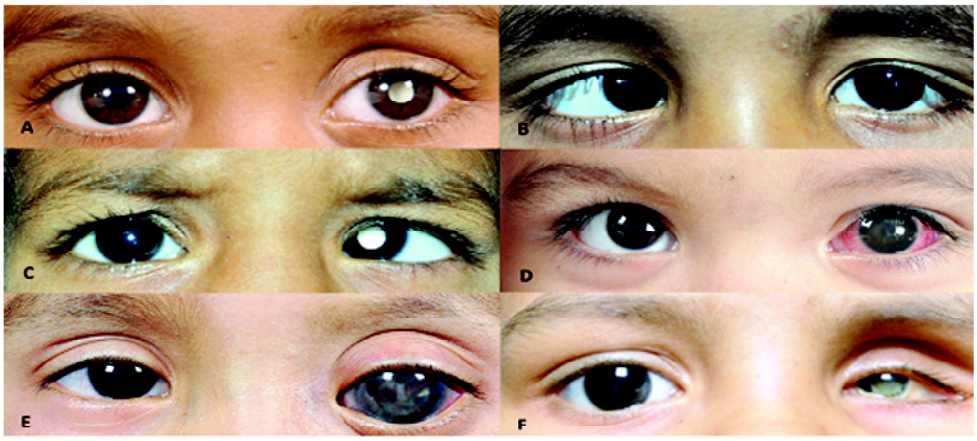

Figure 1: Presenting features of retinoblastoma

(A) White pupillary reflex or leukocoria of the left eye
(B) Strabismus of the right eye
(C) Leukocoria with strabismus of the left eye
(D) Red painful left eye
(E) Enlarged left eyeball
(F) Phthisis bulbi of the left eye

Retinoblastoma presents with a solid retinal tumor, with or without subretinal seeds and / or vitreous seeds. Solid retinal tumors begin as a small translucent thickening of the sensory retina, and gradually enlarge to an opaque yellowish-white lesion with intralesional vascularity and dense chalky white areas of calcification[11]. The lesions can be focal or multifocal. As the tumors enlarge, the tumor cells disseminate into the surrounding tissues with seeding of the tumor in the vitreous (vitreous seeds) and the subretinal space (subretinal seeds). Endophytic tumor growth pattern is associated with vitreous seeds and exophytic tumor growth pattern is associated with retinal detachment and subretinal seeds. Advanced cases can present with extension of the tumor into the anterior chamber (pseudohypopyon), along the optic nerve, and / or with extraocular tumor extension.

Ancillary tests

The most important tool in the diagnosis of retinoblastoma is indirect ophthalmoscopy. The other useful tests include ultrasonography, computed tomography, and magnetic resonance imaging. B-scan ultrasonography reveals a dome shaped or irregular intraocular mass. On A-scan ultrasonography, the noncalcified portion of the tumor demonstrates low to medium internal reflectivity, and the areas of calcium within the lesion exhibit high reflective echoes causing attenuation of the adjacent sclera and orbit[15]. Ultrasonography is also useful to measure the tumor thickness.

Computed tomography (CT) of the orbit helps in the detection of intraocular mass with intratumoral calcification, extension of tumor into optic nerve and extraocular tumor extension. CT orbit is more sensitive in the detection of intratumoral calcification, which is seen as bright hyperdense spots[16]. On magnetic resonance imaging (MRI) of the orbit, retinoblastoma is hyperintense to vitreous on T1, and hypointense on T2-weighted images[16]. MRI is more sensitive in the detection of choroidal and/or optic nerve tumor infiltration. CT and MRI brain are also useful in the detection of pinealoblastoma.

Classification and staging of retinoblastoma

Over the years, several classification systems have been used for retinoblastoma. Intraocular retinoblastoma has been classified using Reese-Ellsworth classification, Essen classification, Philadelphia classification, and International Classification of Retinoblastoma. The most commonly used classification for intraocular retinoblastoma is International Classification of Retinoblastoma (Figure 2), which includes five groups:[17,18]

Group A: Small tumor $\leq$ 3 mm located outside the macula

Group B: Larger tumor > 3 mm or any tumor with associated subretinal fluid or any tumor in the macula

Group C: Tumor associated with focal subretinal and/or vitreous seeds

Group D: Tumor associated with diffuse subretinal and/ or vitreous seeds

Group E: Massive tumor with neovascular glaucoma, opaque media due to intraocular hemorrhage, diffuse infiltrating tumor, aseptic orbital cellulitis, or phthisis bulbi.

For tumors with intraocular and extraocular involvement, the described classifications include Grabowski-Abramson classification, St Jude classification, International Retinoblastoma Staging System, and the TNM (Tumor, node, metastasis) classification.

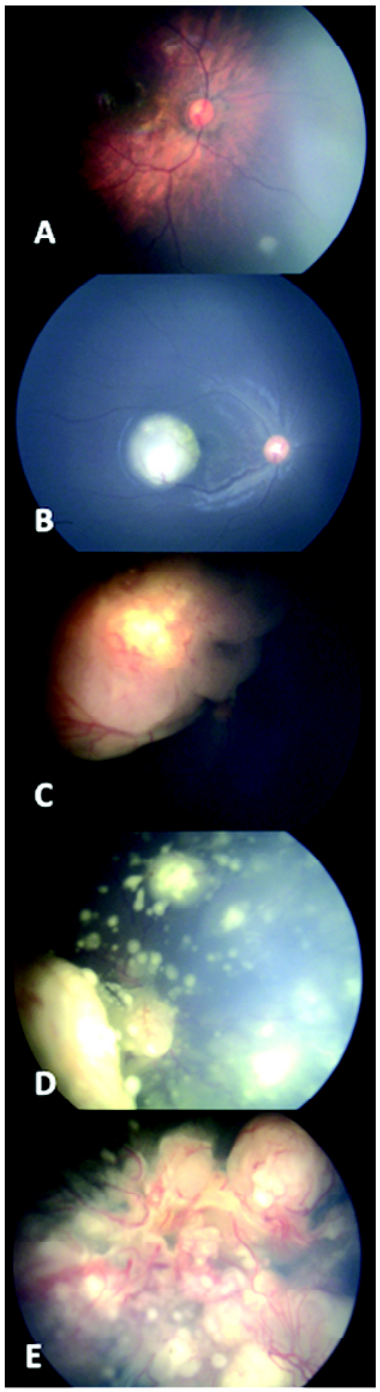

Figure 2: International classification of retinoblastoma
(A) Group A with tumor < 3 mm in size
(B) Group B with tumor > 3 mm in size
(C) Group C with solid tumor associated with focal subretinal seeds
(D) Group D with solid tumor associated with diffuse vitreous seeds
(E) Group E tumor with diffuse tumor filling the globe

The most commonly used classification for extraocular retinoblastoma is International Retinoblastoma Staging System, which includes four stages:[19]

Stage 0 : Intraocular retinoblastoma, eye not enucleated
Stage I : Eye enucleated, no residual tumor
Stage II : Eye enucleated, microscopic residual tumor
Stage III: Local/regional disease
a : Overt orbital disease
b : Local/regional lymph node involvement
Stage IV: Metastatic disease
a : Hematogenous metastasis (without central nervous system (CNS) involvement)
1. Single lesion
2. Multiple lesions
b : Central nervous system involvement
1. Prechiasmatic lesion
2. CNS mass
3. Leptomeningeal and cerebrospinal fluid disease

Treatment of retinoblastoma

The treatment of retinoblastoma depends on the tumor laterality and the tumor grouping/staging. The various forms of treatment for retinoblastoma include:

Local treatment : Laser photocoagulation
Transpupillary thermotherapy
Cryotherapy
Chemotherapy : Periocular chemotherapy
Intravitreal chemotherapy
Intraarterial chemotherapy
Systemic chemotherapy
Radiation treatment : Plaque radiotherapy
External beam radiotherapy
Proton beam radiotherapy
Surgical treatment : Enucleation
Orbital exenteration

Laser photocoagulation

Xenon, Argon, and YAG lasers have been used for laser photocoagulation. Laser photocoagulation can be used for a small tumor < 3 mm in basal diameter and < 2 mm in thickness[20]. The spot size is 200-300 um and the power is 100 to 400 mw. Laser burns are applied around the tumor in a double row fashion. The end point of laser photocoagulation is a grey-white burn. Two to three sessions at 4-week intervals are required to attain tumor

control. The aim of this therapy is to occlude the blood supply to the tumor, to cause tumor regression. Laser photocoagulation should be avoided during systemic/ intrarterial chemotherapy as it decreases the drug delivery to the tumor. With the advent of transpupillary thermotherapy with diode laser, argon laser photocoagulation is less commonly used.

Transpupillary thermotherapy

Transpupillary thermotherapy (TTT) can be used as primary treatment for small tumors (< 3 mm in basal diameter and < 2 mm in thickness) or as consolidation treatment during systemic chemotherapy[21]. 810 nm diode laser is used to achieve hyperthermia and allow tumor destruction. The diode laser can be delivered to the tumor through a microscope adaptor or an indirect ophthalmoscope. When used with indirect ophthalmoscope, the spot size is 1.2 mm and the power is 300 to 800 mw. The laser burns are applied over the tumor. The end point of TTT is a grey-white burn. The preferred duration of treatment during each session is 5 to 7 minutes. Two to three sessions at 4 to 6-week intervals are required to attain tumor control, when used as primary treatment. When combined with systemic chemotherapy (Chemothermotherapy), TTT is performed after 1 to 2 hours of administration of systemic chemotherapy[21]. A mean of 3 to 4 sessions are required to achieve adequate tumor control.

Cryotherapy

Cryotherapy is used to treat small tumors (< 3 mm in basal diameter and < 2 mm in thickness) in the pre-equatorial region. Triple freeze-thaw cryotherapy is advocated in the management of retinoblastoma[22]. Single or triple freeze-thaw cryotherapy at 1 or 2 locations administered 24 hours prior to systemic chemotherapy increases the permeability of carboplatin into the vitreous by 15-folds and thus allows better tumor control[23].

Periocular chemotherapy

Periocular administration of chemotherapy allows delivery of higher concentrations of chemotherapy drugs to the posterior segments of the eye.Periocular chemotherapy is used as an adjunct treatment for eyes with persistent vitreous seeding despite other forms of treatment, in patients with bilateral retinoblastoma with poor prognosis at diagnosis, or in those in whom systemic chemotherapy is contraindicated. The most commonly used drug is carboplatin at a dose of 20mg/2cc. The administration of periocular carboplatin results in higher vitreous concentration of carboplatin by 8 to 10-fold when compared to intravenous administration.[24]

Intravitreal chemotherapy

Intravitreal chemotherapy for retinoblastoma was first investigated in 1960's. However, this technique did not gain popularity due to risk of tumor seeding after any intraocular intervention in retinoblastoma. Recently, intravitreal chemotherapy is being used in the treatment of residual/recurrent vitreous seeds. The most commonly used drug for intravitreal injection is melphalan at a dose of 20-30 ug. The drug is given via the pars plana route and is repeated every 7 to 10 days or every month[25,26].

Intraarterial chemotherapy

Intraarterial chemotherapy for retinoblastoma involves injection of chemotherapeutic agent directly into the ophthalmic artery, thus allowing targeted drug delivery into the eye[27]. It can be used as primary or secondary treatment for retinoblastoma. The most commonly used drug for intraarterial chemotherapy is melphalan at a dose of 5mg/30 cc normal saline. The advantages of intraarterial chemotherapy include :

1. Control of intraocular tumor
2. Resolution of Retinal Detachment
3. Globe salvage
4. Minimal systemic side-effects

Systemic chemotherapy

Systemic intravenous chemotherapy is used for chemoreduction of intraocular tumors to facilitate globe and vision salvage, in orbital extention to control the malignancy prior to enucleation or exenteration, for chemoprophylaxis in eyes with high-risk retinoblastoma to prevent systemic metastasis, and for treatment of metastatic retinoblastoma[28-32]. The most commonly used chemotherapeutic regimen to achieve chemoreduction is vincristine sulfate, etoposide phosphate and carboplatin (VEC) for 6 cycles every 3-4 weeks. The advantages of systemic chemotherapy include :

1. Control of intraocular tumor
2. Resolution of retinal detachment
3. Globe salvage
4. Vision salvage
5. Prevention of pinealoblastoma

6. Prevention of systemic metastasis in high-risk retinoblastoma, and
7. Reduction of long-term second non-ocular cancers.

Plaque radiotherapy

Plaque radiotherapy is used as primary treatment for unilateral solitary tumors and most commonly as secondary treatment for recurrent or residual tumors. The size of the episcleral plaque is planned such as to cover 2 mm margin beyond the tumor basal dimension all around the lesion. The tumor apex dose is 40 Gy with a 2 mm safety margin at the tumor apex. The advantages of plaque radiotherapy include:

1. Control of intraocular tumor
2. Resolution of retinal detachment
3. Globe salvage
4. Shorter duration of treatment
5. Minimal side-effects due to minimal exposure of normal tissue outside the radiation field
6. No risk of second malignancies due to radiation exposure

External beam radiotherapy

External beam radiotherapy (EBRT) was the most common modality of primary treatment for retinoblastoma in the pre-chemotherapy era. With the improved chemotherapeutic options, EBRT is rarely used as primary treatment. Currently, it is reserved for cases with poor response to systemic chemotherapy, eyes with extensive subretinal and/or vitreous seeds not responding to other forms of treatment, as an adjunct treatment in cases with extension of tumor .to optic nerve transection or those with extraocular tumor extension. A total dose of 40 to 45 Gy is delivered to the eye in multiple fractions[33]. Though satisfactory tumor control is achieved with EBRT, it is associated with significant adverse effects such as:

1. Dry eye
2. Radiation induced cataract
3. Radiation retinopathy and/or maculopathy
4. Radiation optic neuropathy
5. Orbital hypoplasia
6. Second malignancies due to radiation exposure in patients with germline mutation

The adverse effects are minimal with the newer modifications of EBRT including 3 dimensional cpnformal radiotherapy and intensity modulated radiation therapy.

Proton beam radiotherapy

Proton beam radiotherapy can also be used for the treatment of retinoblastoma. The indications of treatment are similar to external beam radiotherapy. Tumor control with proton beam radiotherapy is comparable to that achieved with EBRT, and is associated with lower incidence of radiation-induced side-effects.

Enucleation

Prior to the advent of radiotherapy and chemotherapy, enucleation was the most commonly used modality of treatment for intraocular retinoblastoma. Despite recent advances in the management of retinoblastoma, enucleation remains the treatment of choice in cases with advanced tumors. The indications of enucleation include group E tumors, tumors not responding to conservative treatment, and in those eyes with optic nerve and/or extraocular tumor extension after neoadjuvant chemotherapy. Adequate care should be taken during enucleation to avoid perforation of the globe and obtain a long segment of optic nerve.

Following enucleation, the histopathologic features are determined. The high-risk histopathologic features predictive of systemic metastasis include:[34]

1. Anterior chamber seeding
2. Iris infiltration
3. Ciliary body infiltration
4. Massive choroidal infiltration ($\geq$ 3 mm in largest dimension)
5. Combined choroidal and optic nerve involvement
6. Retrolaminar optic nerve involvement
7. Involvement of optic nerve transection
8. Scleral involvement
9. Extrascleral involvement

The patients with high-risk retinoblastoma are treated with 6 cycles of adjuvant systemic chemotherapy at 3-week intervals. In cases with involvement of optic nerve transection, full thickness sclera, and extraocular tissue, additional EBRT is recommended.

Orbital exenteration

Orbital exenteration for retinoblastoma is indicated in those cases with orbital tumor extension. With the advent of systemic chemotherapy, primary orbital exenteration is rarely required. The cases with orbital tumor extension become amenable to enucleation with neoadjuvant

systemic chemotherapy, and exenteration is performed in those cases with persistent extraocular tumor despite systemic chemotherapy.

Prognosis

It is estimated that, worldwide, 3001 to 3376 patients die every year, due to retinoblastoma, of which 2845 to 3201 patients (95% cases) are from Africa and Asia[6]. While the mortality rate due to retinoblastoma is 3 to 5% in developed countries, it is 70% in Africa, and 39% in Asia. With early diagnosis and appropriate treatment, the survival rates of children with retinoblastoma can be improved.

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Review Article

Definition of Acute Kidney Injury

P Sri Ram Naveen

Introduction : Acute kidney injury (AKI) is the abrupt loss of kidney function, resulting in the retention of urea and other nitrogenous waste products and in the dysregulation of extracellular volume and electrolytes. The term AKI has largely replaced acute renal failure (ARF), reflecting the recognition that smaller decrements in kidney function that do not result in overt organ failure are of substantial clinical relevance and are associated with increased morbidity and mortality. The term ARF is now reserved for severe AKI, usually implying the need for renal replacement therapy.
The loss of kidney function that defines AKI is most easily detected by measurement of the serum creatinine, which is used to estimate the glomerular filtration rate (GFR). Three problems are associated with the use of serum creatinine to quantitatively define AKI:

1. Serum creatinine does not accurately reflect the GFR in a patient in whom it is not in steady state. In the early stages of AKI, the serum creatinine may be low, even though the actual (not estimated) GFR is markedly reduced, since there may not have been sufficient time for the creatinine to accumulate. When the serum creatinine is rising, estimates of GFR based on creatinine values will overestimate the true GFR, conversely, estimates of GFR will underestimate the true GFR during recovery of kidney function, when the serum creatinine concentration is declining.

2. Creatinine is removed by dialysis. As a result, it is usually not possible to assess kidney function by measuring the serum creatinine once dialysis is initiated. One exception is when the serum creatinine continues to fall on days when hemodialysis is not performed, indicating recovery of renal function.

3. Numerous epidemiologic studies and clinical trials have used different cut-off values for serum creatinine to quantitatively define AKI.[1]

Prior lack of consensus in the quantitative definition of AKI, in particular, has hindered clinical research, since it confounds comparisons between studies. Some definitions employed in clinical studies have been extremely complex, with graded increments in serum creatinine for different baseline serum creatinine values.[1,2]

Several consensus definitions of AKI have been developed in order to provide a uniform definition of AKI. In 2004, the Acute Dialysis Quality Initiative (ADQI) group, which included expert intensivists and nephrologists, proposed consensus and evidence based guidelines for the treatment and prevention of AKI[3]. Recognizing the need for a uniform definition for AKI, the ADQI group proposed a consensus graded definition, called the RIFLE criteria[3]. A modification of the RIFLE criteria was subsequently proposed by the Acute Kidney Injury Network (AKIN, which included the ADQI group), as well as representatives from other nephrology and intensive care societies [4,5,6]. More recently, the Kidney Disease/Improving Global Outcomes (KDIGO) AKI Workgroup proposed a modified definition, harmonizing differences between the RIFLE and AKIN definitions[7].

RIFLE Criteria : The RIFLE criteria consists of three graded levels of kidney dysfunction (Risk, Injury, and Failure), based upon either the magnitude of increase in serum creatinine or urine output, and two outcome measures (Loss and End-stage renal disease [ESRD]). The RIFLE strata are as follows [3]

Risk: 1.5-fold increase in the serum creatinine, or glomerular filtration rate (GFR) decrease by 25 percent, or urine output <0.5 mL/kg per hour for six hours

Injury: Twofold increase in the serum creatinine, or GFR decrease by 50 percent, or urine output <0.5 mL/kg per hour for 12 hours

Failure: Threefold increase in the serum creatinine, or GFR decrease by 75 percent, or urine output of <0.3 mL/kg per hour for 24 hours, or anuria for 12 hours.

Loss: Complete loss of kidney function (eg, need for renal replacement therapy) for more than four weeks

ESRD: Complete loss of kidney function (eg, need for renal replacement therapy) for more than three months.

The change in serum creatinine was specified as occurring over not more than seven days. Subsequent to publication of RIFLE, it was noted that the change in serum creatinine concentrations do not correlate with the percent decrease in GFR that is cited in the RIFLE classification; a 1.5-fold increase in serum creatinine societies [4,5,6], corresponds to a 33 rather than 25 percent decrease in GFR[8]. More recently, the Kidney Disease/Improving Global Outcomes (KDIGO) AKI Workgroup proposed a modified definition, harmonizing differences between the RIFLE and AKIN definitions[7].

However, given the absence of readily available methods for measurement of GFR when serum creatinine is not in steady state, as is the case during acute kidney injury (AKI), changes in GFR are not included in the Acute Kidney Injury Network (AKIN) classification system, Improving Global Outcomes (KDIGO) AKI classification system, except for the classification of children under the age of 18 years.

The RIFLE criteria correlated with prognosis in a number of studies [8.9,10,11,12,13,14,15,16,17,18] As an example, a systematic review of 13 studies demonstrated a stepwise increase in the relative risk of death in patients who met the RIFLE criteria for various stages of AKI[15]. Compared with patients who did not have AKI, patients in the RIFLE stages of "risk," "injury," and "failure" had increased relative mortality risks of 2.4 (CI 1.94-2.97), 4.15 (CI 3.14-5.48), and 6.37 (CI 5.14-7.9). Despite significant heterogeneity among studies, results from most individual reports were qualitatively similar.

The relative risk for mortality by RIFLE stage, based on change in serum creatinine, does not correlate well with the mortality risk by RIFLE stage, calculated basis of urine output criteria. The observed relative risk was greater in studies that used the creatinine criteria alone compared with those that used both the creatinine and urine output criteria to determine RIFLE stage, with a much smaller increment between the "risk" and "injury" stages using urine output than with creatinine. These results suggest that the calibration between the serum creatinine and urine output criteria for staging is poor.

AKIN Criteria : A modification of the RIFLE criteria was developed by the Acute Kidney Injury Network (AKIN), providing both diagnostic criteria and a staging system for acute kidney injury (AKI)[4,5,6].

Diagnostic criteria - The AKIN diagnostic criteria for AKI specify an abrupt (within 48 hours), absolute increase in the serum creatinine concentration of $\geq$ 0.3 mg/dL (26.4 micromol/L) from baseline; a percentage increase in the serum creatinine concentration of $\geq$ 50 percent; or oliguria of <0.5 mL/kg per hour for more than six hours

The latter two of these criteria are identical to the RIFLE "risk" criteria. The addition of an absolute change in serum creatinine of $\geq$ 0.3 mg/dL was based on epidemiologic data that demonstrated an 80 percent increase in mortality risk associated with changes in serum creatinine concentration of as little as 0.3 to 0.5 mg/dL[19]. Including a time constraint of 48 hours is based upon data that showed that poorer outcomes were associated with small changes in the creatinine when the rise in creatinine was observed within 24 to 48 hours [20,21]. However, it should be recognized that this time frame differed from the seven-day time specified in the RIFLE criteria.

Two additional caveats were proposed by the AKIN group:

✧ The diagnostic criteria should be applied only after volume status had been optimized.

✧ Urinary tract obstruction needed to be excluded if oliguria was used as the sole diagnostic criterion.

Staging system - The classification or staging system for AKI is comprised of three stages of increasing severity, which correspond to the Risk (stage 1), Injury (stage 2), and Failure (stage 3) components of the RIFLE criteria, with the addition of the $\geq$ 0.3 mg/dL increase in serum creatinine to the stage 1 criteria. Loss and End-stage renal disease (ESRD) are removed from the staging system and defined as outcomes.

The AKIN modifications to RIFLE have not substantively changed the classification of patients with AKI or improved its ability to predict hospital mortality[22].

KDIGO modifications to RIFLE and AKIN - The Kidney Disease / Improving Global Outcomes (KDIGO) Clinical Practice Guidelines for Acute Kidney Injury (AKI) included a revision to the definition of AKI while retaining the AKI Network (AKIN) staging criteria [7]. In the KDIGO definition, the time frame for an absolute increase in serum creatinine of $\geq$ 0.3 mg/dL is retained from the AKIN definition (48 hours), while the time frame for a $\geq$ 50 percent increase in serum creatinine reverted to the seven days originally included in the Acute Dialysis Quality Initiative (ADQI) RIFLE criteria.

According to KDIGO, AKI is defined by any of the following:

1. Increase in serum creatinine by ≥ 0.3 mg/dL (≥ 26.5 micromol/L) within 48 hours. or
2. Increase in serum creatinine by ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior seven days; or
3. Urine volume <0.5 mL/kg/h for six hours

The KDIGO criteria only utilize changes in serum creatinine and urine output, not changes in glomerular filtration rate (GFR) for staging, with the exception of children under the age of 18 years, for whom an acute decrease in estimated GFR (eGFR) to <35 mL/min per 1.73 m^2 is included in the criteria for stage 3 AKI. As with the RIFLE and AKIN staging systems, KDIGO suggested that patients be classified according to criteria that result in the highest (ie, most severe) stage of injury. Using the KDIGO criteria, AKI is staged as follows:

Stage 1: Increase in serum creatinine to 1.5 to 1.9 times baseline, or increase in serum creatinine to e"0.3 mg/dL (e"26.5 micromol/L), or reduction in urine output to <0.5 mL/kg per hour for 6 to 12 hours.

Stage 2: Increase in serum creatinine to 2.0 to 2.9 times baseline, or reduction in urine output to <0.5 mL/kg per hour for ≥ 12 hours.

Stage 3: Increase in serum creatinine to 3.0 times baseline, or increase in serum creatinine to ≥ 4.0 mg/dL (≥ 353.6 micromol/L), or reduction in urine output to <0.3 mL/kg per hour for ≥ 24 hours, or anuria for ≥12 hours, or the initiation of renal replacement therapy, or, in patients <18 years, decrease in eGFR to <35 mL/min per 1.73 m^2.

Limitations : Several commentaries have been published raising concerns regarding the use of these criteria to diagnose acute kidney injury (AKI), although all commentaries stress the importance of a consensus approach for research purposes[23,24].

In a commentary on the Kidney Disease/Improving Global Outcomes (KDIGO) AKI guidelines, the European Renal Best Practice (ERBP) working group agreed that AKI be defined on the basis of either a change in creatinine or reduction in urine output. The ERBP group recommended that the first documented serum creatinine be used as the baseline, rather than using historical creatinines (ie, prior to the acute illness) or a calculated value based on a presumed baseline glomerular filtration rate (GFR) of 75 mL/min [23]. The ERBP work group also recommended that urine output be assessed per shift using ideal body weight rather than true weight.

Another important issue is the use of urine output as a sole criterion for AKI. By all criteria discussed above, stages are defined by either change in serum creatinine or urine output. However, the assignment of the corresponding changes in serum creatinine and changes in urine output to the same strata is not based on robust evidence. Studies that have examined the prognostic and diagnostic utility of urine output have yielded variable results. As an example, in one assessment of the RIFLE classification, which compared the serum creatinine and urine output criteria, the serum creatinine criteria were strong predictors of intensive care unit (ICU) mortality, whereas the urine output criteria did not independently predict mortality[13]. Another study, however, has suggested that urine output may be a more sensitive marker for AKI than serum creatinine[26].

The KDOQI and ERBP groups have offered opinions on the use of urine output as a criterion for AKI[23,24]. The ERBP group stressed the importance of using both urine output and the serum creatinine and stated that, although all criteria included the urine output, in practice, it is often omitted from studies[23]. The KDOQI working group noted that brief durations of oliguria do not prognostically correlate with small changes in the serum creatinine and may just reflect insufficient volume resuscitation[24]. Until this issue is resolved, it is reasonable to use the criteria that result in the least favorable strata, as suggested in the Acute Dialysis Quality Initiative (ADQI) group[3] and affirmed by KDIGO.

The determination of a baseline creatinine for individual patients is another issue that has been raised as a potential criticism. It is impossible to calculate the change in serum creatinine in patients who present with AKI, but without a baseline measurement of serum creatinine. The authors of the RIFLE criteria had initially suggested back-calculating an estimated baseline serum creatinine concentration using the four-variable MDRD equation, assuming a baseline GFR of 75 mL/min/1.73 m^2 [3]. However, this approach has been demonstrated to result in significant misclassification [23] and should not be utilized. As noted above, the ERBP group recommended that the first documented serum creatinine be used as the baseline, rather than using historical creatinines (ie, prior to the acute illness) or a calculated value based on a presumed baseline GFR of 75 mL/min[23].

A more global concern raised by the KDOQI work group is that the use of a definition based upon a biomarker, such as serum creatinine, or a variable, such as urine output, may result in a marked increase in the number of nephrology consultations, which would provide uncertain benefit to the patient [24]. As noted by an accompanying editorial to the KDOQI commentary, discretion is required to determine the clinical significance of a diagnosis of AKI [27]

Clinical Utility : The clinical utility of these criteria is uncertain. This issue has been raised by both a multidisciplinary work group convened by KDOQI and the Canadian Society of Nephrology[24,25]. These criteria have greatest utility in epidemiologic studies and in defining consistent inclusion criteria and/or endpoints for clinical studies.

It seems likely that these criteria will eventually be replaced, at least in part, by sensitive and specific biomarkers of renal tubular injury. The use of such biomarkers, analogous to troponin as a marker of myocardial injury, will permit development of a new paradigm for classifying acute kidney injury (AKI) that is not solely dependent upon serum creatinine or other functional markers.

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Review Article

Balloon Dacryoplasty: Indications, Techniques and Outcomes

Mohammad Javed Ali MD, FRCS

Abstract: Balloon dacryoplasty is a term used for a set of minimally invasive lacrimal procedures that utilize specially designed balloons, targeted at different points in the lacrimal system for a wide range of indications. Balloons were first used by Becker and Berry in 1989. This article would review the details of various balloons, instruments needed, indications in pediatric and adult populations, preoperative preparations, operative standards and procedures, postoperative managements and outcomes.

Key Words : Baloon Dacryoplasty, Minimally invasive, Lacrimal procedure

Introduction

Balloon dacryoplasty is a term used for a set of minimally invasive lacrimal procedures that utilize specially designed balloons, targeted at different points in the lacrimal system for a wide range of indications. Balloons were first used by Becker and Berry in 1989.[1] Around the same time Munk et al reported balloon catheter dilatation for adults with epiphora using an angioplasty catheter under fluoroscopic guidance.[2] There are ongoing efforts worldwide to look for an alternative to dacryocysto-rhinostomy (DCR) in the management of nasolacrimal duct congenital nasolacrimal duct obstructions (CNLDO) and adult partial nasolacrimal duct obstructions.

This gave impetus to the exploration of balloons in form of 9 mm balloon DCR for primary and revision cases, 5 mm balloon dilatation for internal ostium stenosis and 2 or 3 mm balloon dilatation for alternative to dacryocystorhinostomy (DCR).

This article would review the details of various balloons, instruments needed, indications in pediatric and adult populations, preoperative preparations, operative standards and procedures, postoperative managements and outcomes.

Balloons and Instruments

A good nasal endoscopic set up is ideal for a balloon dacryoplasty. A typical Balloon dilatation set (Atrion Corporation, Allen, Texas, USA) (Fig 1) consists of the following:

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a) 2 mm, 3mm, 5mm or 9mm balloon catheters
b) Inflation device
c) Lacrimal probes
d) Punctum dilator
e) Dandy's nerve hook
f) Intubation set with retrieval device

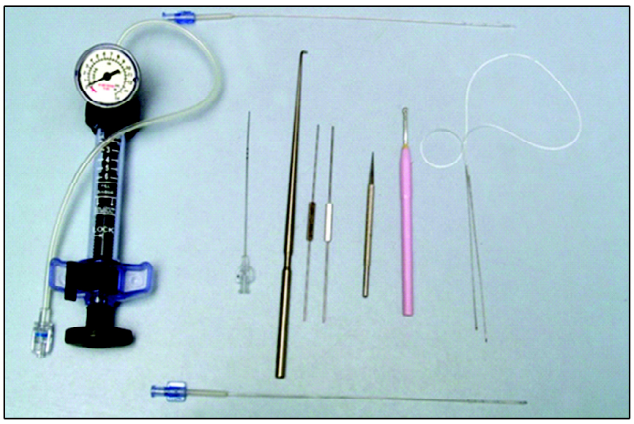

Fig 1: A complete balloon dacryoplasty set. Note the presence of the 2 mm catheter.

Balloon catheters are specially designed with an inflatable balloon at one end of the catheter and hub with luer-lock mechanism at the other which engages the inflation device. 2 mm balloons catheters are named so since they have an outer diameter of 2 mms during an inflated stage (Fig 1). The length of this balloon is 13 mms. Similarly 3mm balloon has an outer diameter of 3mms but the length is 15 mms. The 5 mm (Fig 2) and 9mm (Fig 3) balloons have outer diameters of 5 mm and 9 mm respectively but their length is 8 mms. 9 mm balloon catheter is much sturdier and is angulated at 120 degrees focused within the balloon segment. Two important markings on the 2mm

and 3 mm catheters is the 10 mm and 15 mm black marks to serve as a guide when the catheters are within the nasolacrimal ducts (Fig 1).

The inflation device has a manometer which displays the pressure reading in atmospheres (Fig 1). Proximal end of the manometer has a tube with a luer-lock adaptor for attachment to the catheters and the distal end has a locking device and a knob. When the locking device is to the left, it indicates an unlocked stage, whereas if it is to right, it indicates a locked stage. The knob when rotated clockwise with the manometer in locked stage, steadily increases the pressure within the device and inflates the balloon whereas its anti-clockwise rotation reduces the pressure and thus deflates the balloon. Preoperative and Intraoperative nasal endoscopic examination is essential for these procedures.

Fig 2: A 5 mm balloon catheter.

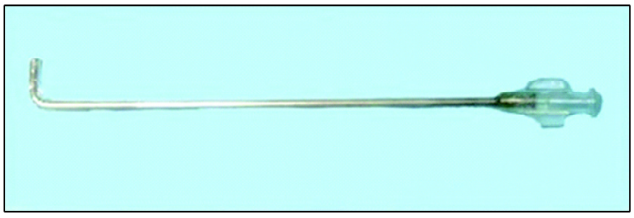

Fig 3: A 9 mm balloon catheter

Balloon Dacryoplasty in Children

Syringing and Probing has been a standard of care for congenital nasolacrimal duct obstructions (CNLDO). Although it is a good procedure with high success rate, the same is not true for older children.[3-4] Probing is less effective in older children because of complex blocks or diffuse narrowing of the nasolacrimal duct.[5-6] Silicone intubations are generally carried out in older children or those who fail probing but the drawbacks of these procedures in children including stent prolapse, second sitting for removal of tubes and keeping them in-situ for 2-3 months need to be taken into account.[7]

Balloon dilatation came into vogue because it achieves true dilatations of narrowed segments, easier to perform than primary silicone intubation with good success rates. A 2 mm balloon is used for patients less than 30 months of age and 3 mm for children more than 30 months of age. The indications of balloon dacryoplasty for congenital nasolacrimal duct obstructions[1,6,8,9] are:

a) Failed Probing

b) Failed intubation

c) Older children (>12 months of age)

d) Down's syndrome or any syndromic association with CNLDO

Surgical technique

Preoperative preparation includes decongestion of the inferior meatus with 0.05% Oxymetazoline. 2 drops can be placed half an hour before the procedure or alternatively a cottonoid soaked with the drug can be placed in inferior meatus for 5 minutes before the procedure. Following dilatation of the puncta, a probing is performed as a standard procedure and the probe is inspected in the inferior meatus to confirm that all the blocks are overcome. An I-probe (Quest Medical Inc, Allen, Texas, USA) can be used which is similar to a bowman's probe with a small eyelet near the tip to wash off the debris following probing and also to reflect on the free flow following probing. Inferior turbinate medialization may occasionally be needed along with probing if it appears to be impacted to the lateral wall.

The sleeve of the balloon is removed, it is then lubricated with either a viscoelastic or a 1% CMC (carboxymethycellulose) drops and gently placed into the lacrimal system just like the procedure of probing and introduced further into the nasolacrimal duct till the 15 mm mark is adjoining the puncta or the balloon exits just beyond the valve of Hasner as seen with nasal endoscopy (Fig 4). In the meantime the inflation device filled with saline or fluorescent stained saline should be ready in the locked position. The air should be removed from the device after saline filling. The luer-lock hub of the inflation device is connected to the catheter and the knob is slowly rotated in the clockwise direction by the assistant while the surgeon can be visualizing the dilatation of the balloon via the endoscope.

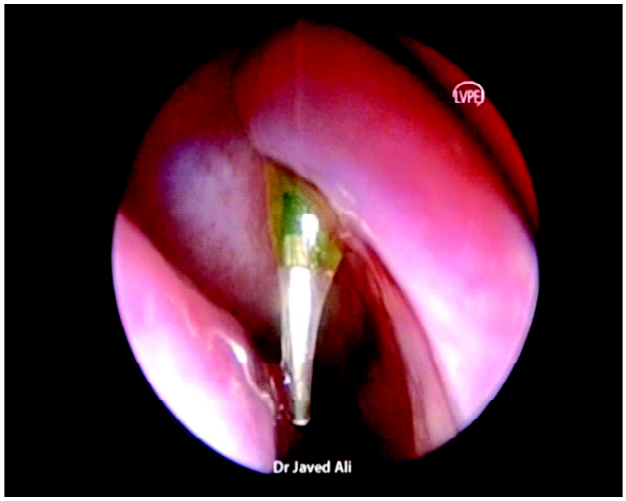

Fig 4 : Endoscopic view of the naso- lacrimal duct dilation using a 3 mm balloon catheter.

The balloons are inflated to 8 atmospheres of pressure for duration of 90 seconds. The inflated balloon should be under constant monitoring in the nose (Fig 4). The knob of the inflation device is then rotated in an anti-clockwise manner to deflate the balloon. Once deflated, without disturbing the catheters position, it is re-inflated to 8 atmospheres for 60 seconds. The balloon is again deflated and pulled back till the 10 mm mark adjoins the punctum or the tip of the balloon is barely visible proximal to valve of Hasner. The two cycles of inflation and deflation are carried out again in this position. The catheter and the inflation device are then disconnected followed by gentle withdrawal of the catheter from the lacrimal system. The lacrimal passages are then irrigated with either saline or fluorescein stained saline. The fluid should flow easily and in copious amounts indicating success of the procedure. The saline from the inflation device is then emptied after unlocking the device.

The author practices the use of intravenous dexamethasone 4 mg during surgery. Post-operatively, topical steroid-antibiotic (Tobramycin-Fluormethalone) combinations are given in tapering doses over 2 weeks. Patients are examined at 6 weeks and 3 months and the outcome measures that are looked for is tear meniscus height, relief in symptoms, and occasional dye disappearance test. Numerous publications have classified the outcomes as excellent if the child has complete resolution of epiphora with normal tear drainage, good if the child has minimal residual symptoms with minimally delayed dye disappearance test, fair if there are moderate residual symptoms or delayed dye clearance and poor if there is no improvement.[1-11]

Outcomes

Balloon dacryoplasty for congenital nasolacrimal duct obstruction is a very effective treatment modality for specific indications as mentioned already. The success rates range from 76% to 83% in various large case series.[8-11] Tien DR[8] following his study of 39 lacrimal systems observed that balloon catheter dilatation is simple and atraumatic and should be considered as an alternative to silicone intubation in patients who undergo probing. Tao S et al[9] studied 73 lacrimal systems of CNLDO undergoing balloon catheter dilatation with patients whose mean age was 35.6 months. 39 (53%) of these were failed probing or post silicone intubation. The overall success rate was 76.7% but it was very interesting to note that children undergoing secondary dilatation following failed previous procedures did not show a statistically significant difference (P = 0.8165) in outcomes when compared to the primary group. Therefore it was concluded that balloon catheter dilatation appears to be successful especially for older children who fail probing or silicone intubation. Leuder et al[10] studied the outcomes of balloon dacryoplasty in 76 children above the age of 18 years. Though the procedure did not appear to benefit simple obstructions more than probing, it however was beneficial in 82% (n=28) of the patients who had stenosis of the distal nasolacrimal duct. Leuder et al[11] further studied the efficacy of balloon catheter dilatation in 32 children with persistant congenital nasolacrimal duct obstructions (CNLDO) following previous failed attempts at recanalization. Outcomes were found to be excellent and good in 28% and 47% of the patients respectively. Yuskel et al[12] studied the efficacy of balloon dilatation in older children with a mean age of 43.9 months with a mean follow up of more than 25 months and reported success rates of close to 90%. The concept of balloon dacryoplasty for older children especially post probing is steadily gaining rapid ground as an alternative to silicone intubation and dacryocystorhinostomy. The authors of the present study are conducting a study in older children who failed probing earlier. A combination of balloon dilatation and silicone intubation is performed and the initial results appear to be promising, however long term results would ascertain its efficacy.

Balloon Dacryoplasty in Adults

There has been a renewed interest in using minimally invasive approaches for partial and complete nasolacrimal

duct obstructions in adults. This led to increased attention to the use of balloon-assisted lacrimal surgeries in adults. We will discuss this under 2 headings, Partial NLD obstructions and complete NLD obstructions

Partial Nasolacrimal Duct Obstructions

Incomplete NLDO's are usually managed with a dacryocystorhinostomy. With the advent of balloons several studies have looked at the efficacy of using 3 mm balloon dilatation in such cases. The procedure is similar to what has been described above for pediatric dacryoplasty except that probing needs to be much more meticulous to overcome the multiple blocks or diffuse narrowing of the nasolacrimal ducts. This is followed by a primary intubation under endoscopic guidance. The authors usually use Crawford tubes or I-Stents (Quest Medical Inc, Allen, Texas, USA) and retain them for 12 weeks before removal.

Perry JD et al[13] reported a success rate of 73% after treatment with balloon dilatation and intubation for partial obstructions in adults. Kuchar A et al[14] reported an overall success of 90% in improvement of symptoms in adults and 56% experiencing complete resolution of epiphora. The authors in their unpublished study of 21 partially obstructed nasolacrimal ducts of 12 patients have shown an anatomical patency of 71% and functional success of 62%, 6 months after removal of stents. The later parts of this study have shown an additional benefit of doing balloon dacryoplasty under dacryo-endoscopic guidance.

Complete Nasolacrimal Duct Obstructions - EBA DCR

For complete obstruction, Endoscopic Balloon assisted Dacryocystorhinostomy (EBA-DCR) using the 5 mm or more commonly the 9mm is an alternative to standard external or endonasal DCR's. One difference that needs to be kept in mind here is that unlike the 5 mm balloon which is used via the trans-canalicular route, the 9 mm can only be used transnasally (Figs 2 and 3). The authors use 5 mm balloon catheter only for revision DCR's and the 9 mm balloon catheter for both primary and revision DCR's. There is very scanty literature on the use of 3 mm balloons targeting the completely obstructed nasolacrimal ducts in adults.[14-16] Song et al[15] and Janssen et al[16] found initial failure rates ranging from 41-44%, however others like Kuchar et al[14] found a failure rate of 10.7% at the end of one year. The clinical use of 3 mm balloons targeting the completely obstructed nasolacrimal ducts is very limited and generally not followed, but such patients are being increasingly managed by the 9mm balloon assisted primary endoscopic DCR.

9 mm primary endoscopic balloon DCR Primary endoscopic DCR using the 9 mm balloon catheter (Fig 2) is a good alternative to an external or endoscopic DCR. It was introduced and popularized by Silbert DI.[17] The advantages of this procedure include

a) Reduced operative trauma
b) Less bleeding
c) Faster and less time consuming
d) No need for powered endoscopic instruments
e) Less post-operative morbidity
f) Early rehabilitation
h) High success rates

Surgical Technique

Good case selection is vital for the success of any surgery and so is true for 9 mm endoscopic balloon DCR. Suspicion of any lacrimal sac tumor, severe deviated nasal septum and canalicular obstruction are contraindications, the former being an absolute and latter two being relative. Anesthesia can be general or monitored anesthesia care with sedation. Once the patient is under anesthesia, lidocaine 2% with adrenaline combination is injected in nasal sub mucosal plane, 2-3 cc, anterior and inferior to the axilla of the middle turbinate. The nose is then packed with cottonoids soaked in 0.25% Oxymetazoline, placed under the middle turbinate and in front of its insertion with the help of bayonet forceps, preferably under endoscopic guidance.

Once the patient is draped, the nasal pack is removed and the puncta are gently dilated progressively to allow number 3 or 4 reinforced bowman's probe to be passed into the lacrimal sac. The probe is directed towards the infero-posterior part of the lacrimal fossa, since it is very thin and can be easily overcome. Once the bone is overcome, the position of the middle turbinate is assessed and if needed a mild medialization of the middle turbinate is carried out. The probe is then passed inferiorly and superiorly in a honeycomb pattern initially followed by opening of the lacrimal sac in a 'filleting open' motion. A blakesly forceps is then introduced into this small opening and pulled back into the nose with its mouth wide opened. Bits of tissues around now can be gently removed. The 9

mm balloon catheter is now connected to the inflation device and introduced into the nose with the balloon end going in first. Under the guidance of the bowman's probe, the catheter is introduced into the newly made ostium and inflated to 8 atmospheres for 90 seconds. It is then pulled into the nose backwards with the balloon still inflated (Fig 5). The balloon is deflated, introduced into the ostium again and reinflated for 60 seconds and again pulled back in the inflated state. This makes the ostium very big and fragments of bone and mucosa are then removed. Once the ostium is of adequate size, intubation is carried out with Crawford tube or the specially designed large diameter Stent tubes. The nose is then packed using cellulose sponges.

Soon following the surgery a single intravenous dose of 8 mg dexamethasone is administered. Postoperatively the patient is placed on systemic antibiotics, topical antibiotic-steroid combinations, nasal decongestant and saline nasal douching. The patient is reviewed at 1 day, 1 week, and 3 months. The tubes are retained for 12 weeks. The outcome measures that are looked for is tear meniscus height, relief in symptoms, and occasionally dye disappearance test. Routine syringing is not practiced by the authors unless patient complains of epiphora.

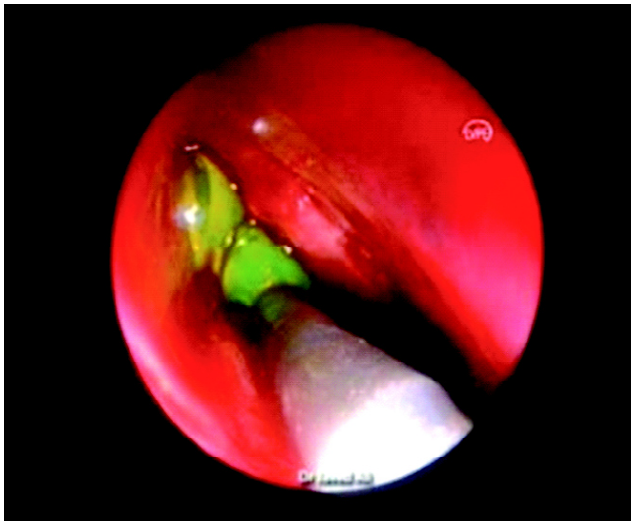

Fig 5: Endoscopic view of a 9 mm primary EBA DCR.

Outcomes

The results of primary endoscopic 9 mm balloon DCR's in long term are appearing to be quite encouraging. Silbert DI[17] in a large case series of 97 patients reported success rates of 92%. Among the 8 cases which failed in this series, 3 underwent repeat surgery, one of them with 5 mm balloon and were successful.[17] Longer follow up with still larger number of patients will ascertain its efficacy in long run.

Balloon Assisted Revision DCR

Revising a failed DCR is a challenging job. For primary external and endoscopic DCR, the failure rate has been reported to be 5-10% or less and 10-20% or less, respectively.[18-19] The most common cause of a DCR failure is occlusion of the rhinostomy site by soft tissue or cicatricial closure of the Ostium. The stenotic or occluded DCR fistula is amenable to balloon dilatation. It is of advantage since the occlusion is primarily a soft tissue and the bony window is usually adequate. The authors use both 5 mm and 9 mm balloon catheters for their failed external or endonasal cases.

The 5 mm catheters (Fig 2) are usually used for very early failures where there is usually a stenotic fistula. A bowman's probe is passed to identify the area in front of the common canaliculus and to clear any soft tissue. The 5 mm balloon catheter is then inserted through the upper canaliculus and under endoscopic guidance, the DCR fistula is enlarged with the standard inflation (Fig 6) and deflation cycles are discussed already. Following dilatation of fistula, any soft tissues in the vicinity are gently removed, mitomycin c 0.04% is applied, followed by Crawford intubation. The 9 mm balloon catheter is also used in the same fashion as already described for primary DCR. Though long term studies are not available, the initial results in the unpublished author series look promising. What needs to be stressed is identification of all the etiological factors contributing to the DCR failure and addressing them adequately yields satisfying results.

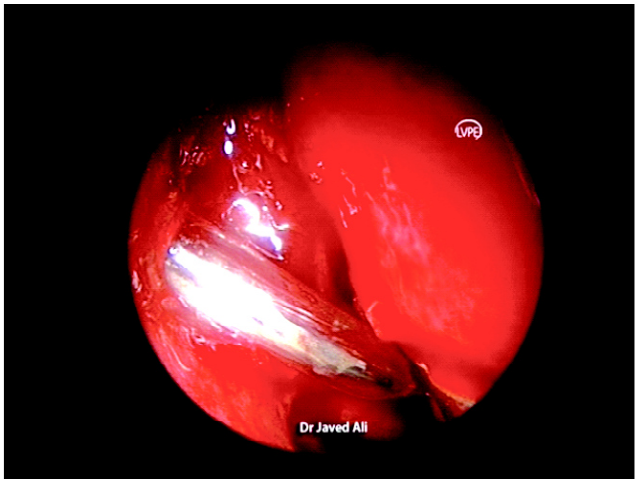

Fig 6 : Endoscopic view of the DCR ostium enlargement using a 5 mm balloon.

Conclusions

Balloon dacryoplasty and Balloon-assisted primary and revision DCR's are speedily gaining grounds in minimally invasive lacrimal surgeries with increasing indications for their use. These techniques are essential in the armamentarium of a dacryologist. Careful patient selection and skillful nasal endoscopy are important factors for successful outcomes.

A good clinical armamentorium along with constant innovative habits helps facing challenges thrown by lacrimal disorders thrilling and profitable.

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Original Article

Efficacy of Bronchial Wash and Brush Cytology and its correlation with Biopsy in Lung Lesions

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Abstract : Back ground : Lung cancer is the commonest cause of cancer related deaths worldwide. So early diagnosis and management is the key to prevent mortality. Bronchoscopic guided washing and brushing can complement histological biopsy in early diagnosis as it is having good cytological yield. The aim of this study is to evaluate the efficacy of bronchoscopic washings, brushings and its correlation with subsequent biopsy in diagnosing lung lesions. Materials and methods : Prospective study of 38 cases from 20 to 70yrs of age was conducted in department of pathology, MIMS from Jan 2013 to Dec 2013. They had visible endobronchial lesions by flexible bronchoscopy and subjected to cytological washing and brushing study and subsequent biopsy. Cytological and biopsy specimens were fixed in isopropyl alcohol and formalin respectively and stained with Hemotoxylin & Eosin stain. Results : Cytology revealed 12 malignant,13 benign,5 suspicious and 2 inadequate smears respectively. Histopathology of these cases confirmed 23 as malignant and 14 as benign. True positive were 16 and true negative were 13 cases. 1 false positive case and 6 false negative cases were reported. The bronchial wash cytology showed sensitivity of 80.5%, specificity of 92.85% and accuracy of 80.5%. Conclusion : Bronchial cytology is a valuable tool and yields almost same information as biopsy.

Key Words : Bronchial washings, Biopsy, Lung Cancer

Introduction : Lung cancer is currently the most frequently diagnosed and the common cause of cancer related mortality worldwide. The increasing incidence could be due to increase in smoking, change in life style, increased environmental pollution and also the availability of different modern diagnostic modalities to detect lung cancer.

Similarly, pulmonary tuberculosis still remains a leading cause of death in developing countries.

To treat the disease successfully, it should be diagnosed at earliest possible stage. For early diagnosis different diagnostic modalities are available which include; radiology, bronchoscopy, bronchial biopsy, brushing, washing cytology. It is not possible to perform all techniques in each patient because each has specific advantages and disadvantages. However their combined use yields the best results.[1-3]

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Bronchial biopsies cannot be performed in more peripheral sites or in patients at risk of haemorrhage. So alternative methods for diagnosis are sometimes required. Bronchoscopic washing, brushing may complement tissue biopsies in the diagnosis of lung lesions[4, 5]. The bronchial washing is a safer technique. There is still disagreement as to the value and reliability of wash and brush cytology in comparison with histology for the diagnosis of malignancy. An attempt has been made to determine whether a combination of biopsy procedure is more effective than a cytological methods in both neoplastic and non-neoplastic lung lesions.[6, 7]

Materials and Methods : A prospective study of 38 patients was done from January to December 2013 in Department of Pathology, MIMS. The samples for cytological and histological examination were collected from the patients with pulmonary signs and symptoms and their radiology and bronchoscopic examination suggested a lung mass. The samples were obtained by flexible fibreoptic bronchoscopy done in the Department of pulmonary medicine, Maharajahs Institute of Medical Sciences.

The bronchial wash material was obtained from the bronchial tree by instilling 30 to 50 ml of isotonic saline and re-aspirating it. All the samples were preserved in 50% ethyl alcohol. The specimens were centrifuged for five minutes at a rate of 1500 revolutions per minute. Slides were prepared from cell concentrate and stained with H&E stain. The smears were grouped into malignant, benign, suspicious and unsatisfactory/inadequate category. Bronchial brushings were obtained by the use of a stiff-bristle disposable brush.

Brushing material was smeared directly on to at least three clean glass slides and stained with H&E stain. Biopsy was done with regular cup-forceps, fixed in formalin and paraffin embedded sections were stained with H/E stain. Special stains like AFB (acid fast bacilli), PAS (periodic acid Schiff) was done wherever necessary.

Results : Samples from 38 patients were evaluated with a male to female ratio of 6:1.The mean age of presentation was 45 to 60yrs in both males and females.

Cytological examination revealed 12 malignant cases along with 5 suspicious cases (Table-1). Out of these 5 suspicious cases, 4 proved to be malignant on histopathology. So these 4 cases were included in true positive cases. Only one case with suspicious report showed features of squamous metaplasia, so included in false positive category. 13 cases were labeled as true negative because these were confirmed on biopsy also as benign. 6 smears were false negative because cytologically these were benign and on histology proved to be malignant.

The benign cases were diagnosed as tuberculosis (5), aspergillosis (1) and non specific inflammation (13).Cytological typing of tumor(Pie chart) showed 11 cases to be squamous cell carcinoma, 1 case as adenocarcinoma. 2 smears on cytology came as insufficient or inadequate. Out of these 2 inadequate smears 1 proved as squamous cell carcinoma histopathologically.

On biopsy examination (Table-2), 23 cases (60.52%) were malignant whereas 14(36.8%) cases were proved as benign. Among the malignant cases, squamous cell carcinoma were 21 and adenocarcinoma were 02. In the category of benign lesions, chronic granulomatous inflammation was noted in 6 cases (4 tuberculous lesion and 2 as aspergillosis) and 8 cases were revealed as acute and chronic non specific inflammation.

The bronchial cytology revealed a sensitivity of 72.72%, specificity of 92.85% and an accuracy of 87.5%. As far as malignant and benign lesions are concerned, complete cytological and histological correlation was observed in 29 cases (80.5%) (Table-3).

Table-1 Types of lesion on cytology (n=38)

Non neoplastic lesion	19
Neoplastic lesions	12
Suspiscious	05
Inadequate	02

Table-2 Types of lesion in biopsy (n=38)

Non neoplastic lesion	14
Neoplastic lesions	23
Inadequate	01

Table-3 Comparison of cytological and biopsy results (n=38)

Diagnostic Category	Cytology	Biopsy
Non neoplastic lesion	19	14
Neoplastic lesions	12	23
Suspiscious	05	-
Inadequate	02	01

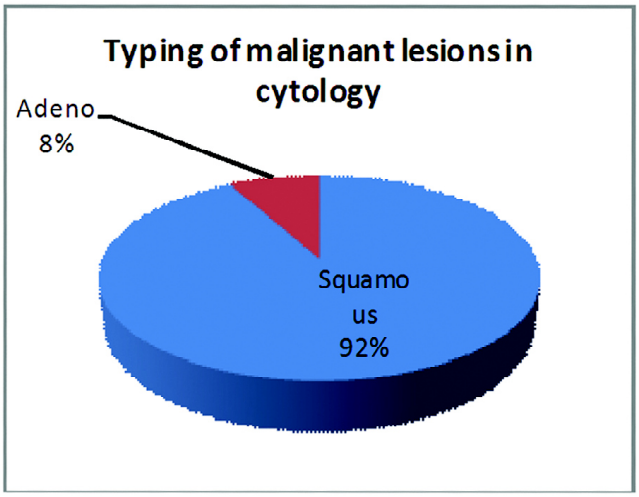

Table-4 Comparison of cytological and biopsy results (n=38)

		Cytology	Histology
Benign	Tuberculosis	05	04
	Aspergillosis	01	02
	Nonspecific inflammation	13	08
Malignant	Squamous cell carcinoma	11	21
	Adenocarcinoma	01	02
	Suspscious	05	0
Inadequate	Sample	02	01

Discussion : Lung tumors are the most common cause of death due to cancer in men and are now emerging as an important cause of cancer related mortality in females.[8]The male to female ratio in this study was 6:1 which is closer to other studies[9]. Majority of these cases were found in their 5th and 6th decades. This could be due to higher prevalence of smoking in males in our society. The objective of present study is to assess the sensitivity and specificity of bronchoscopic cytological procedures; bronchial washing and brushings, comparing them with biopsy of lung lesions .The first realization that cancer of the lung could be accurately diagnosed and typed by the microscopic study of expectorated cells is generally attributed to Dudgeon and Barret.[10]

Fibreoptic bronchoscopy was introduced in 1968 as a diagnostic procedure. Since then apart from sputum, different methods for obtaining satisfactory specimens have become available. The specimens collected by fiberoptic bronchoscope yield a higher positive rate. The sensitivity of bronchial aspirates in diagnosing lung cancers has been 75 to 88.1 % by various studies.[7,11] The bronchial secretion smear cytology that was used previously was discontinued because of lack of representative smears. Now bronchial brushings are favored for the cytological investigation of proximal lung cancers. From management point of view, lung tumors are generally separated into small cell carcinomas and non small cell carcinomas. For small cell carcinomas intensive chemotherapy is advised whereas the non-small cell carcinomas are better treated surgically. More than 80% cases have been correctly typed by Truong and co-workers with sputum, washing or brushing cytology.[12]

In our study only one case was false positive which is less than the study by Tanwani and Haque.[9]This false positive case was due to squamous metaplasia along with dysplasia. False positivity may occur due to misinterpretation by the cytopathologist due to chronic inflammatory cells, epithelioid cells, atypical histiocytes or squamous metaplasia. These false positive cytological results may have serious consequences for the patients in which biopsy is not possible due to risk of haemorrhage or anatomical obstruction. Therefore it is advisable to under diagnose suspicious/atypical smears.

Out of 38, six cases were false negative in the present study which is higher than the previous study.[9]The reasons for false negative results could be superadded inflammation, non representative sample or hypocellular aspirates. In this study the accurate correlation between histological and cytological results was found in 29 of 36 cases (80.5%) which is similar to the study by Naryshkin and Daniel.[13] In another two studies this correlation was 81.8%[14]and 88.4%[11] respectively. The diagnostic efficacy of cytology in our series showed 80.5% sensitivity and 92.85% specificity which is comparable to a study by Jay and colleagues.[15] The overall accuracy of bronchial cytology was 75% and 75.4% by two other studies by Truong et al[12] and Chaudhary et al[16] respectively, whereas in present study it was slightly higher (85.3%). As for as the typing of lung tumor on cytology is concerned, it was 92% which compared to another study where it was 90%[17]but histopathology revealed 100% accuracy in typing of lesion that is more than the cytological typing (92%) (table-4).The difficulties in specifying the tumor on cytology can be lack of cell groups, keratinisation, mucus production and scant cellular material. In our series the frequency of suspicious smear was3% whereas Spjut etal[18] reported it as 10%. Out of 5 cases with a suspicious cytologic report in our series, four were diagnosed as malignancy in biopsy (squamouscell carcinoma) which is lower to another study at USA (1995) where 94% suspicious cases proved to be malignant on histology.

Conclusion

Pulmonary wash and brush cytology has excellent sensitivity, specificity and accuracy. It yields almost same information as biopsy and is particularly useful in patients with evidence of obstruction or risk of haemorrhage.

It is quite safe, economical and an experienced cytopathologist is necessary for interpretation of smears. But regarding individual typing of lesions, biopsy is more effective than cytological study. The combination of endobronchial cytology with biopsy can be considered as the best procedures for the diagnosis of lung cancer during bronchoscopy.

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Original Article

Correlation of Carotid Intima-Media Thickness with Atherosclerosis in Diabetes

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Abstract : B-mode ultrasound of Common Carotid artery at its bifurcation for measure of the Carotid intima-media thickness (CIMT), offers a valid non-invasive quantifying test for macro-vascular complications like atherosclerosis. **Material and Methods**: 50 cases of type 2 Diabetes and 30 age and sex matched Non-diabetics controls were taken for present study and subjected to Ultra-sonographic scanning of the carotid arteries using B-mode color Doppler imaging to calculate CIMT. **Observation**: In the study group, the relationship between CIMT with triglycerides, LDL-C and total cholesterol are positively correlated ($p<0.01$) which is statistically significant, whereas with CIMT and HDL-C the relation is negatively correlated, which is statistically significant ($p<0.01$). **Conclusion**: This study focuses on the importance of CIMT as a simple, non-invasive, safe and cheap screening test for assessing the risk of macro-vascular complications like atherosclerosis as evidenced by strong correlation between CIMT and Lipid Abnormalities in type 2 Diabetes Mellitus patients.

Key Words : B-Mode USG, CIMT, Atherosclerosis

Introduction : The most important change in early subclinical period of atherosclerotic disease are endothelial dysfunction and increase in intima-media thickness observed in all arterial beds. Thickening of arterial wall of the common carotid artery and plaque formation at the carotid bifurcation are observed in preclinical atherosclerosis as macro-vascular complications[1].

The intima-media thickness (IMT) of the carotid artery is highly correlated with cardiovascular events in Type 2 Diabetes Mellitus (T2DM) [2]. CIMT has been shown to be independently associated with CAD in Indian subjects and is a well standardized surrogate marker for assessing cardiovascular risk[3]. Thus B-mode ultrasound of common carotid artery at its bifurcation to measure for intima-media thickness offers a valid non-invasive quantifying test for atherosclerosis and is a better alternative to carotid angiography for detection of atherosclerosis and its progression[4]. Hence it is rapidly becoming an acceptable method to detect generalized atherosclerosis[5]. CIMT have been successfully used as a "window" or indicator for generalized and coronary atherosclerosis[6, 7].

Materials and Methods : 50 cases of T2DM with duration of more than 2 years, with age more than 35 years , of either sex, receiving oral hypoglycaemic agents or insulin or both, out-patients or in-patients under the department of Medicine, Maharajah's Institute of medical sciences, Nellimarla, during the period of November 2011 to October 2013 were included. 30 age and sex matched non-diabetics constituted the controls of the present study. Patients with systemic hypertension, with history of smoking, on ACE/ARB's, Type 1 DM and secondary diabetes were excluded. All patients included in the study underwent detailed clinical history analysis, physical examination and necessary investigations like HbA1C and Lipid profile. Routine tests for infection like DC, TLC, Urine, Chest X-ray, ESR were carried out. Ocular fundus examination and estimation of Microalbuminuria by Micral test were done. Both Common Carotid arteries were examined. Ultrasonographic scanning of the carotid arteries was performed using a high resolution B-mode colour Doppler imaging and an electrical linear transducer was used. Scanning of extra cranial common carotid or internal carotid arteries in neck was performed bilaterally according to evading edge of second echogenic line.

Results : In the study group comparison of total cholesterol with CIMT showed statistically positive correlation (correlation coefficient 'r'=0.606, $p<0.01$) and also in control group,significant positive correlation was found between total cholesterol and CIMT (correlation coefficient 'r'=0.676, $p<0.01$). The present study group

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which showed significant positive correlation ($p<0.01$) between LDL-C and CIMT is very much comparable to previous studies. In the present study group a positive correlation is found between triglycerides and progression of CIMT (correlation coefficient 'r'=0.838) which was statistically significant ($p<0.01$). The values in control group were very much similar to study group (correlation coefficient 'r'=0.698, $p<0.01$ statistically significant). But in the study group, progression of CIMT had negative correlation with HDL-C (correlation coefficient 'r'= -0.689, $p<0.01$) which is statistically significant.

Table-1 : Comparing different factors in study and control groups

Factors	Study group Mean± SD	Control Group Mean± SD	t-test	p-value	Significance
CIMT	1.196± 0.301	0.97± 0.29	3.22	<0.01	HS
Age	60.44± 10.26	57.37± 7.85	1.53	>0.05	NS
BMI	25.41± 4.73	23.17± 2.69	2.69	<0.01	HS
W/ H/ ratio	0.939± 0.112	0.96± 0.044	0.84	>0.05	NS
FBS	154.6± 55.1	124.33± 14.8	3.69	<0.001	VHS
PPBS	216.1± 73.01	167.43± 23.41	4.35	<0.001	VHS
TG	199.96± 63.1	139.46± 51.1	4.72	<0.001	VHS
LDL-C	137.9± 35.1	120.17± 48.98	2.08	<0.05	S
HDL-C	38.64± 2.85	38.9± 5.95	0.22	>0.05	NS
Total-C	192.92± 37.7	168.1± 45.5	2.54	<0.01	HS

Discussion : CIMT is a well established index of atherosclerosis that correlates with prevalent and incident coronary artery disease[6]. Studies have shown a relationship between atherosclerosis in the carotid and coronary arteries. Furthermore statistically significant correlations (range 0.3-0.5) between CIMT and coronary atherosclerosis the latter based on a coronary angiogram, coronary calcium studies, or intravascular ultrasound have been noted[7].

The progression of CIMT is influenced by cardiovascular risk factors and is directly related to the risk of future cardiovascular events.

The prospective, community-based Framingham Heart Study provided rigorous support for the concept that hypercholesterolemia, hypertension, and other factors correlate with cardiovascular risk. Abnormalities in plasma lipoproteins and derangements in lipid metabolism (increased LDL, TG, Cholesterol and Decreased HDL) rank among the most firmly established and best understood risk factors for atherosclerosis. As this study clearly establishes Positive correlation between CIMT and LDL, TG, Cholesterol and Negative Correlation between CIMT and HDL in a stastically significant manner, it implies a strong evidence of correlation between CIMT and Coronary as well as Generalised Atherosclerosis. As patients with type 2 diabetes mellitus suffer unduly from premature and severe atherosclerosis affecting coronary, cerebral and carotid arteries, ultrasonographic assessment of easily accessible arteries like carotid arteries have been advocated as a surrogate marker over less accessible vessels such as coronary and cerebral arterial systems in diabetic populations.[1]

Summary : In the study group the relationship between CIMT with triglycerides, LDL-C and total cholesterol are positively correlated ($p<0.01$) which is statistically significant whereas CIMT and HDL-C the relation is negative correlation which is statistically significant ($p<0.01$). Hence this study focuses on the importance of CIMT as a simple, non-invasive, safe and cheap screening test for assessing the risk of macrovascular complications in type 2 DM patients and hence the risk of CAD a common cause of mortality in Diabetic population.

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Original Article

CBNAAT: a Novel Diagnostic Tool For Rapid And Specific Detection Of Mycobacterium Tuberculosis In Pulmonary Samples

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Abstract : Mycobacterium tuberculosis remains to be one of the most significant causes of death from an infectious agent. Rapid diagnosis of tuberculosis and detection of Rifampicin (RIF) resistance are essential for effective disease management. CBNAAT (Cartridge Based Nucliec Acid Amplification Test) also known as Gene Xpert MTB/RIF assay is a novel integrated diagnostic device for the diagnosis of tuberculosis and rapid detection of RIF resistance in clinical specimens. We determined the performance of the MTB/RIF assay for rapid diagnosis of tuberculosis and detection of rifampin resistance in smear-positive and smear-negative pulmonary specimens obtained from possible tuberculosis patients. Aim of the study - To assess diagnostic usefulness of Gene Xpert MTB/RIF assay technique in management of tuberculosis. Material and Methods : This is an Observational study conducted in the department of pulmonary medicine Maharajah's Institute of Medical Sciences, Vizianagaram between June 2012 and December 2013. Two hundred and five Sputum samples were obtained from Tuberculosis suspects. All samples were tested on Gene Xpert for MTB/RIF detection after AFB microscopy. Results : 108(52.68%) sputum samples were AFB smear positive and 96 (47.32%) were negative. In MTB/RIF assay 144 (70.24%) were MTB positive and 61 (29.76%) were negative. Chi-Square test was applied; P value is <0.001. All results are highly significant. The MTB/RIF assay also detected 4 RIF-resistant specimen and 140 RIF-susceptible specimens, and the results were confirmed by drug susceptibility testing. Conclusions: The MTB/RIF test is a simple method, and routine staff with minimal training can use the system. It helps to avoid injudicious use of anti-tuberculosis drug.

Key Words : AFB, Gene Xpert, MTB/RIF, TB and ZN staining.

Introduction

The global burden of TB remains enormous. More than 9 million new M tuberculosis (MTB) cases and 1.7 million deaths occur annually worldwide. Most of them occur in resource-limited settings.[1] Smear microscopy for acid-fast bacilli (AFB) is rapid and inexpensive.

Smear microscopy is the cornerstone for the diagnosis of TB in resource-limited settings but it has only modest (35-80%) sensitivity and a poor positive predictive value (PPV)[2]. Culture is the "gold standard" for final determination, and also permits drug susceptibility testing. However, it remains largely inaccessible in resource-limited settings as a result of infrastructure and financial limitations. Even where accessible, culture results are typically not available for 2-6 weeks. Diagnosis through either smear or culture requires multiple steps that significantly impede program effectiveness. The need is for accurate, feasible, rapid, affordable, and if possible, near-point-of-case TB diagnostic tests for use in resource-limited settings.

Drug resistance is a major issue in the treatment of tuberculosis. Though rare for Rifampicin (RIF) , drug resistance is common in other 1st line drugs Isoniazid (INH), Ethambutol (EMB), and Pyrazinamide (PZA).[2] Multi drug resistance is a reflection of either mismanagement of tuberculous patients wrong diagnosis, delay in diagnosis, wrong or interrupted treatment and mistreatment of both first and second line drugs. Injudicious use of drugs is to be avoided in the better interest of patients[3]. Thus, for rapid identification, which is essential for earlier initiation of treatment and improved outcomes, more effective public health interventions and newer methods of detection are required[4]. Multiple approaches to improve diagnosis of TB are in development. One test, Gene Xpert® MTB/RIF, which was recently endorsed by the World Health Organization (WHO), has the potential to lead a revolution in the diagnosis of active TB disease and multidrug-resistant (MDR) TB.

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Gene Xpert test is a semi-quantitative nested real-time PCR in-vitro diagnostic test with two uses:

(1) The detection of Mycobacterium tuberculosis complex DNA in sputum samples or concentrated sediments prepared from induced or expectorated sputum that are either acid-fast bacilli (AFB) smear positive or negative.

(2) The detection of Rifampicin resistance associated mutations of the rpoB gene in samples from patients of Rifampicin resistance[5, 6].

Among the most important diagnostic techniques the Gene Xpert is one which detects gene mutation (rpoB) associated with RIF resistance. Hence it is of enormous importance in the diagnosis of both drug susceptible and drug resistant cases. Gene Xpert test can be performed on sputum or bronchial washing samples. Results become available in less than 2 hours. The rapid detection of Mycobacterium tuberculosis and its resistance to Rifampicin (RIF's) allows the physician to make critical decisions in the management of patient regarding therapy during the same visit.

The aim of this study is to determine the diagnostic usefulness of the MTB/RIF assay for the diagnosis of tuberculosis and rapid detection of rifampicin resistance in smear-positive and smear-negative pulmonary clinical specimens.

Materials and Methods : This is an observational study conducted in the department of Pulmonary medicine, Maharajah's Institute of Medical Sciences during June 2012-December 2013. CBNAAT, an automated instrument (figure 1) which works on the principle i.e., sample processing, nucleic acid amplification, and detection of the target sequences in simple or complex samples using real-time PCR and reverse transcriptase PCR.

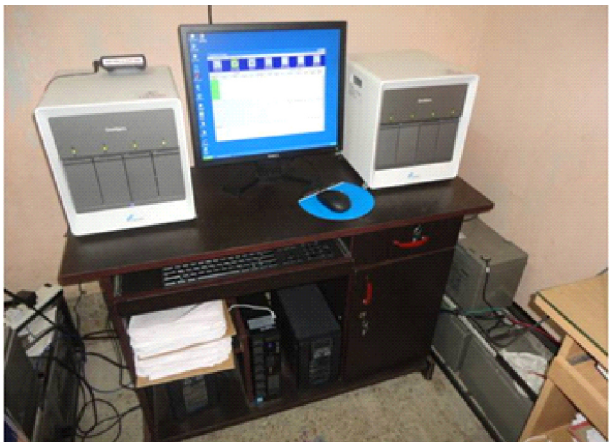

Figure 1 : CBNAAT instrument

205 Patients who presented with symptoms and signs suggestive of pulmonary tuberculosis, chest X ray showing features of pulmonary tuberculosis were included in the study. Sputum samples from these patients were sent for AFB staining as well as Xpert MTB/RIF test. Early morning, deep coughed sputum specimens in sterile containers were included in the study. Specimens were stored at 2-8°C in freezer till further processing. However, the specimen can be safely stored at 35°C for three days. After collection, Ziehl-Neelsen (ZN) staining was done on all samples in department of Microbiology and each sample was run on Gene Xpert.

Standard Assay Procedure of Gene Xpert: The assay utilizes single-use plastic cartridges with multiple chambers that are preloaded with liquid buffers and lyophilized reagent beads necessary for sample processing, DNA extraction and heminested rt-PCR.[7,8]Clinical sputum samples (or decontaminated sputum pellets) are treated with sodium hydroxide and isopropanol-containing sample reagent (SR). The SR is added to the sample (currently recommended at a 3:1 ratio for sputum pellets and a 2:1 ratio for unprocessed sputum samples) and incubated at room temperature for 15 min. The treated sample is then manually transferred to the cartridge which is loaded into the Gene Xpert instrument.

Subsequent processing is fully automated. The cartridge incorporates a syringe drive, a rotary drive and a filter upon which M. tuberculosis bacilli are deposited after being liberated from the clinical material. The test platform employs a sonic horn that inserts into the cartridge base to cause ultrasonic lysis of the bacilli and release of the genetic material. The assay then amplifies a 192 bp segment of the rpoB gene using a hemi-nested rt-PCR reaction[8,9]. Mycobacterium tuberculosis is detected by the five overlapping molecular probes (probes A–E) that collectively are complementary to the entire 81 bp rpoB core region[8, 9].

M. tuberculosis is identified when at least two of the five probes give positive signals with a cycle threshold (CT) of d"38 cycles and that differ by no more than a prespecified number of cycles. The basis for detection of rifampicin resistance is the difference between the first (early CT) and the last (late CT) M. tuberculosis-specific beacon (ÄCT). The system was originally configured such that resistance was reported when ÄCT was >3.5 cycles and sensitive if d"3.5 cycles.

Results

ZN staining was done for 205 samples of the patients who were having history suggestive of pulmonary tuberculosis. Out of these 108(52.68%) sputum samples were AFB smear positive and 96(47.32%) were negative. (Table 1) Then all the samples were tested on Gene Xpert ® MTB/RIF assay. Out of the 205 sputum samples of the patients having history suggestive of pulmonary tuberculosis, 144 (70.24%) were MTB positive and 61 (29.76%) were negative. The MTB/RIF test detected the agent in 108 out of 109 sputum smear positive cases, and 36 out of 96 sputum smear negative cases.

Table 1.

Gene Xpert	Sputum for AFB+Ve	Sputum for AFB-Ve	Total samples
MTB +ve	108	36	144
MTB - ve	1	60	61
Total samples	109	96	205

The results of Gene Xpert and ZN staining are compared in our study. It is evident from the table that Gene Xpert MTB/RIF is more useful than ZN staining. As compared to ZN staining it can detect MTB even in 1ml of sputum.

The second important advantage of Gene Xpert is that it also detects Rifampicin (RIF) resistance and helps us to diagnose multi-drug resistance tuberculosis (MDR TB). In table2. 4 patients were rifampicin resistant out of 205 (1.9%) suspected cases, which was confirmed with drug susceptibility.

Table 2.

RIF Resistance	MTB+Ve	MTB-Ve	Total samples
NOT DETECTED	105	96	201
DETECTED	4	0	4
Total samples	109	96	

Statistical Analysis : All results were analyzed statistically by applying chi-square test. P value was <0.001 and all the results are highly significant

Discussion

In this study, the performance of the MTB/RIF assay with pulmonary specimens obtained during the clinical routine was compared with AFB staining. In our study, the MTB/RIF test detected the agent in 144 out of 205 pulmonary specimens (70.24 % detection rate) whereas sputum for AFB was able to detect only 108 out of 205 pulmonary specimens (52.68% detection rate). Out of 109 sputum smear positive cases, tuberculosis was detected in 108 cases, by MTB/RIF test and out of 96 sputum smear negative cases 36 cases were detected.

A previous study found that the MTB/RIF assay had a calculated limit of detection of 131colony-forming units(CFU)/ml of sputum and was able to detect as few as 10 CFU/ml of sputum in 35% of samples compared with approximately 10,000 CFU/ml with conventional smear microscopy[10].

The MTB/RIF test is easy to perform and is less dependent on the user's skills. Routine staff with minimal training can use the test. Technicians can be trained in 1-2 days; Only 2 steps (addition of buffer and sputum sample) are manual and the rest of the steps are automated,The results are available within 90 minutes. Each table top-sized module can process 4 samples daily (larger modules can run 200 tests in an 8-hour day), and because it is a closed system, biosafety and contamination concerns are minimized. It has a short turn-around time and simultaneously detects M. tuberculosis and RIF resistance in less than 2 hours. Although the MTB/RIF test could be a useful tool for rapid identification of RIF-resistant M. tuberculosis, especially in smear-positive clinical samples, the test results must always be confirmed by culture and DST.

Conclusion

We concluded that as compared to sputum AFB microscopy, Gene Xpert is more sensitive and specific not only for acid fast bacilli (AFB) detection but also for rifampicin (RIF) resistance. Routine staff with minimal training can use this system. It also helps to avoid injudicious use of anti-tuberculosis drugs.

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Original Article

A Study of Co-Morbidity in Mental Retardation

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Abstract : Mental retardation (MR) is a condition of arrested or incomplete development of the mind, characterized by impairment of skills (cognitive, language, motor and social) manifested during the developmental period, which contribute to overall level of intelligence. Intellectual Disability is a more precise term (used in DSM-V). MR is an etiological factor for development of various co-morbidities, which account for substantial burden of the disease. However, the extent of this co-occurrence varies substantially between reports. Aim: To study the prevalence of psychiatric and medical comorbidity, among different degrees of Mental Retardation. Settings and Design: This is a cross-sectional, single-centered study conducted at the out patient department of Psychiatry, Maharajah's Institute Of Medical Sciences. Material & Methods : Sixty-three persons, who came for disability certification, were diagnosed with MR as per ICD-10 criteria, The Wechsler's Adult Intelligence Scale – IV and The Developmental Screening Test for IQ and Vineland Social Maturity Scale for SQ assessment were used. Psychiatric and medical co-morbidities were diagnosed, using clinical examination, laboratory investigation, the ICD-10 Diagnostic criteria and CHA-PAS SCALE. Statistical Analysis : The statistical analysis was done by using the Statistical Package for Social Sciences (SPSS) 13.0 version. Frequency, percentages and chi square analysis were used to analyze the data. Result : Out of 63, 40 were found to have medical co-morbidity, while 38 were found to have psychiatric co-morbidity. Severe and profound MR was almost always associated with medical co-morbidities, while mild to moderate MR with psychiatric illness. Different co-morbid disorders were analyzed and discussed. Conclusions : Evaluation and diagnosis of co-morbid disorder in different degrees of MR is of paramount importance in order to modify treatment schedules and improve the patient outcomes.

Keywords : Mental retardation, psychiatric co-morbidity, medical co-morbidity

Introduction

There is evidence of recognition and treatment of intellectual disability that dates back to Hippocrates, Galen & the Middle Ages. The modern history for the field of intellectual disability begins in the late 18th century [1]. The term co-morbidity indicates co-existence of an index disease with another clinical entity. It is increasingly recognized that co-morbidity is more common among people with intellectual disabilities than among the general population. It has now been clearly documented that the mentally retarded are at a greater risk of developing psychiatric disorders (Borthwick- Duffy & Eyman, 1990) [2] and medical illness. Dual diagnosis refers to the joint occurrence of mental retardation and psychiatric disorders. The rates of dual diagnosis have varied from 31% to 100% across various studies (Jacobson, 1982) [3]. Indian review of results of previous studies on co-morbidities stressed on mood disorder (8%), hyperkinetic disorder (14%), autism (11%), psychosis (11%), conduct disorder (2%) enuresis (2%) and unspecified emotional and behavioral disorder (26 %)[4], mostly not based on any scale but rather the examiners expertise and the ICD-10 & DSM-IV diagnostic guidelines. A Taiwan study using a structured questionnaire indicated that nearly half (47.7%) of the subjects with MR had an associated co-morbid medical or psychiatric illness. A population-based study using a Learning Disability Register in the UK reported that the prevalence of epilepsy was 26% in adults with intellectual disabilities. In view of the common interface of medical and mental-health problems in mentally retarded, initiatives should be taken to enhance their healthcare following a multidisciplinary approach, laying emphasis on dual diagnosis and diagnostic overshadowing. Since there is inconsistency among various reports of occurrence of co-morbidities in MR, this study has been conducted.

Aims & Objectives

To study the prevalence of psychiatric and medical comorbidity, in persons with different degrees of mental retardation.

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Materials and Methods

This is a cross-sectional, single-centered study conducted in the Psychiatry Out-Patient Department of a tertiary care General Hospital, from February 2013 to May 2013. Sixty three persons, who came for disability certification, were taken into the study after obtaining the informed consent from the concerned. The data was recorded in a semi-structured proforma and included socio-demographic profile, primary assessment including case history, complete physical and mental status examination. All subjects included in this study were between 5 years and 60 years.

Diagnosis of mental retardation was made as per ICD-10 classification. The degree of retardation was assessed based on the intelligence quotient and social quotient by using the following tests:-

Developmental Screening Test[5] : It was developed by Bharath Raj (1977, 1983) and consists of 88 items, which represent the behavioral characteristics of respective age levels, from birth to 15 years of age. At each age level, items are drawn from behavioral areas, like motor development, speech, language, and personal-social development. Appraisal of the child can be done in semi-structured interview with a parent. The IQ calculator incorporated with the test folder helps in ready computation of IQ from mental age and the chronological age. DST showed very high positive correlation +0.7215 to +0.9968 with other intelligence or developmental tests. Inter-scorer reliability (+0.928) and test retest reliability (+0.98) were also found to be high and satisfactory.

The Wechsler Adult Intelligence Scale - IV[6] : It is a standardized scale developed by David Wechsler and revised by Pearson and was released in 2008. It is composed of 10 core sub-tests and five supplemental sub-tests, with the 10 core sub-tests comprising the Full Scale IQ. It measures IQ in individuals aged 16–90 years. It takes 60-90 minutes to evaluate. The web based evaluation and scoring option was used to interpret the index and sub-test level scale scores.

Vineland Social Maturity Scale-Indian Adaption[7]: It was developed by J Bharath Raj Mallin and was published in 1984. It is an 89-item questionnaire assessing 4 domains. It takes 20-40 minutes to administer and evaluates the social age, social quotient and adaptive functioning ranging from 0 -15 years. E.A. DOLL originally devised the VSMS in 1935 and since then this test is being used in many parts of the world. The administration should be carried out in a semi-structured informal atmosphere. At the end of assessment Full and Half credits may be counted. If the total score falls exactly on the last item of an age level, the patient is given the full Social Age at that age level. The procedure for obtaining the Social Age from the Raw is as follows.

S.Q = (Social Age / Actual Age) X 100

The interpretations of S.Q are on similar lines as that of I.Q Except that S.Q has a social life reference. Research studies (Goulet and Barelay 1962)[16], have shown a consistent and high correlation between VSMS Social Age (S.A) and the Stanford Binet M.A DOLL reported a correlation of + = 0.85 and Patterson (1943) reporting a correlation of + = 0.96 with the Binet scale on a sample of normal children.

The patients were divided into 4 groups depending on the degree of retardation, as per ICD-10, which were as follows: -

A. Mild Mental Retardation (IQ range 50 to 69)
B. Moderate Mental Retardation (IQ range 35 to 49)
C. Severe Mental Retardation (IQ range 20 to 34)
D. Profound Mental Retardation (IQ range less than 20)

All these were evaluated for the presence of any co-morbid psychiatric illness using the CHA-PAS scale and ICD-10. The Child and Adolescent Psychiatric Assessment Schedule (CHA-PAS)[8] is a semi-structured clinical interview developed by Steve Moss, Robin Friedlander and Pauline Lee, first published in 2007. It is a 97-item questionnaire covering 8 domains, namely anxiety disorder, depressive episode, manic episode, OCD, psychosis, ADHD, conduct disorder and autism spectrum disorder. It is a four-point scale constructed around ICD-10 and DSM-IV criteria, with strong diagnostic indications. The CHA-PAS score form enables two different clinical episodes to be rated on the same form with a provision to interview a second informant to generalize findings. It uses a scoring system that provides a single score for each diagnostic category and each of the categories has a corresponding threshold. If the person reaches or exceeds the threshold it is probable that they warrant a diagnosis in that category. Due to age disparity and to maintain uniformity this scale was selected. Other psychiatric disorders were diagnosed based on the ICD-10 criteria.

A complete physical examination with necessary laboratory investigations was than to assess the presence of co-morbid medical conditions like epilepsy, infectious diseases, hearing impairment, tuberous sclerosis, cerebral palsy, bowel & bladder incontinence, hypothyroidism, recurrent fever, orthopedic handicap, cleft lip & cleft palate, plexiform neurofibromatosis, mucopolysaccharidosis, sexual dysfunction, asthma and enuresis.

Ethical approval

Informed consent was obtained from parents or legal representatives, and the study has been approved by the Ethical Board of the tertiary care institute.

Data Analysis

The statistical analysis is done by using the Statistical Package for Social Sciences (SPSS) 13.0 version. Frequency, percentages and chi square analysis were used to analyze the data. The following results were drawn.

Results

Demographics and Prevalence

The study sample constituted of 63 patients, out of which 29(46%) were of mild MR, 9(14.3%) of moderate MR, 12(19%) of severe MR and 13(20.6%) were of profound MR (Table-1).

Thirty four (53.9%) patients were males and 29 (46.1%) were females, 39(61.9%) were below 18 years while 24 (38.1%) were above 18 years (Table 1). Profound MR was more common in the below 18 age group.

TABLE 1 : SOCIO DEMOGRAPHIC PROFILE IN DIFFERENT DEGREES OF MR

		MILD	MODERATE	SEVERE	PROFOUND	TOTAL
GENDER	**MALE**	(16) 25.4%	(4) 6.3%	(9) 14.3%	(5) 7.9%	(34) 53.9%
	FEMALE	(13) 20.6%	(5) 7.9%	(3) 4.7%	(8)12.7%	(29) 46.1%
AGE	**BELOW 18**	(17) 27%	(4) 6.3%	(6) 9.5%	(12) 19.1%	(39) 61.9%
	ABOVE 18	(12) 19.1%	(5) 7.9%	(6) 9.5%	(1) 1.6%	(24) 38.1%
TOTAL		(29) 46%	(9) 14.3%	(12) 19%	(13) 20.6%	(63) 100%

A total of 52 (82.53%) were diagnosed with a co-morbid disorder, while 11(17.46%) patients had no co-morbid illness. Twenty-six (41.26%) patients had both psychiatric and medical illness, 14 (22.22%) had only medical co-morbidity while 12 (19.06%) had only psychiatric co-morbidity (Figure 2). Psychiatric co-morbidity was present in 38 (***P=0.975***) patients out of which 17(44.7%) belonged to mild, 6(15.8%) to moderate, 7(18.4%) to severe and 8(21.1%) to profound MR. Forty(***P=0.030***) patients had a medical disease out of which 16 (40%) were associated with mild MR, 3(7.5%) with moderate, 10(25%) with severe and 11(27.5%) with profound MR, (Table 2, Figure 1,2,3).

FIGURE 1 : OVERVIEW OF PREVALENCE OF PSYCHIATRIC & MEDICAL CO-MORBIDITY

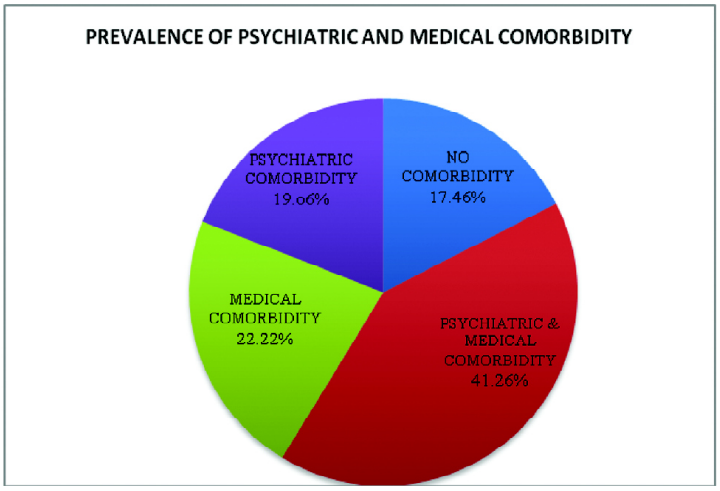


TABLE 2 : PREVALENCE OF CO-MORBIDITY IN DIFFERENT DEGREES OF MR

	MILD	MODER-ATE	SEVERE	PRO-FOUND	TOTAL	CHI-SQUARE
MEDICAL COMORBIDITY	(16) 40%	(3) 7.5%	(10) 25%	(11) 27.5%	(40) 100%	VALUE-8.938 DF-3 SIG- 0.030
PSYCHIATRIC COMORBIDITY	(17) 44.7%	(6) 15.8%	(7) 18.4%	(8)21.1%	(38) 100%	VALUE-214 DF- 3 SIG- 0.975
NO COMORBIDITY	(6) 54.5%	(2) 18.2%	(2) 18.2%	(1) 9.1%	(11) 100%	VALUE-1.217 DF- 3 SIG- 0.749

FIGURE 2 : PREVALENCE OF CO-MORBIDITY IN DIFFERENT DEGREES OF MR

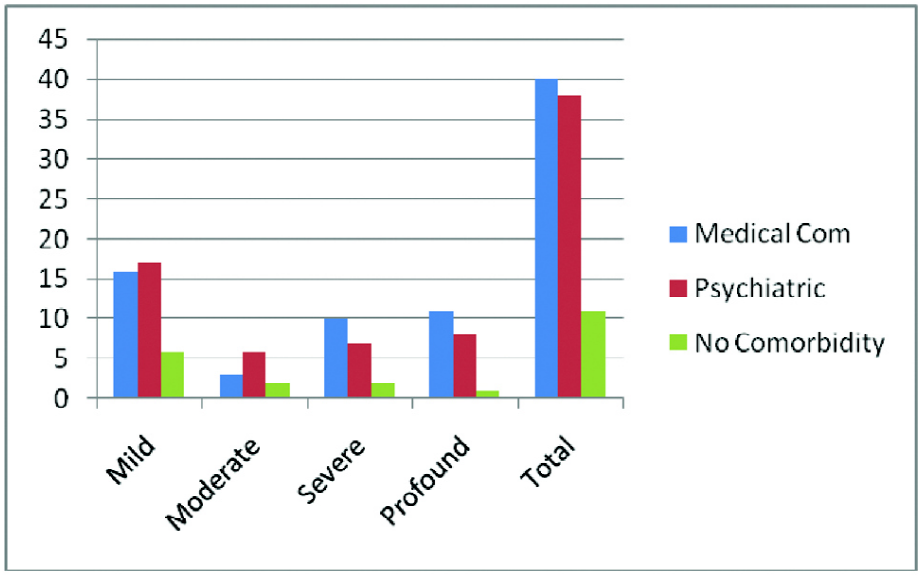
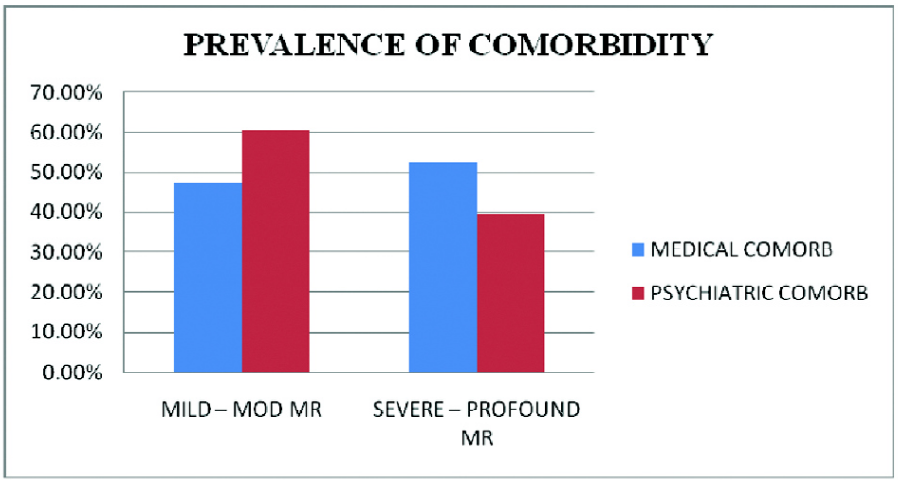


FIGURE 3 : PREVALENCE OF CO-MORBIDITY IN DIFFERENT DEGREES OF MR



Most frequently seen psychiatric co-morbidity was Stereotyped Movement Disorder (36.85%) followed by Conduct Disorder (23.7%) and ADHD (18.42%). The frequency of Stereotyped Movement Disorder and Autism Spectrum Disorders (10.52%) was more in severe to profound MR, while Conduct disorder, Psychosis (2.63%), OCD (5.26%), Depressive episode (8%), Manic episode (5%) and Anxiety disorders (13%) were common in mild to moderate MR. ADHD was seen equally across mild, moderate and severe MR and less in profound MR. Eating Disorders (5.26%) and PTSD (5.26%) were associated with mild and severe MR, while Separation Anxiety Disorders (5.26%) with mild and profound MR. Habit and Impulse Disorders (2.63%) and Tic disorder (2.63%) were seen in moderate MR (Table 3, Figure 4).

The most common medical co-morbidity seen was epilepsy (45%) followed by cerebral palsy (15%). Other frequently seen medical co-morbidity was cleft lip & cleft palate (7.5%), asthma (10%) and recurrent fevers (7.5%). Epilepsy was seen across all degrees of MR but more common in Mild & Sever MR. Recurrent Fever was diagnosed equally across mild, severe & profound MR, Cleft Lip & Cleft Palate across mild, moderate & profound MR, Asthma & cerebral palsy across mild & profound MR while orthopedic handicap (5%) was equally associated with mild & severe MR. Enuresis (5%) and Plexiform neurofibromatosis (2.5%) were diagnosed in profound MR while rare syndromes like Mucopolysaccharidosis (5%) was seen in severe MR. Infectious diseases (2.5%), Hearing impairment (2.5%), tuberous sclerosis (2.5%), hypothyroidism (2.5%) and bowel & bladder incontinence (5%) were found in Mild MR. Sexual dysfunctions (2.5%) was seen in moderate MR. (Figure 5, Table 4).

FIGURE 4 : FREQUENCY DISTRIBUTION OF VARIOUS PSYCHIATRIC DISORDERS IN DIFFERENT DEGREES OF MR

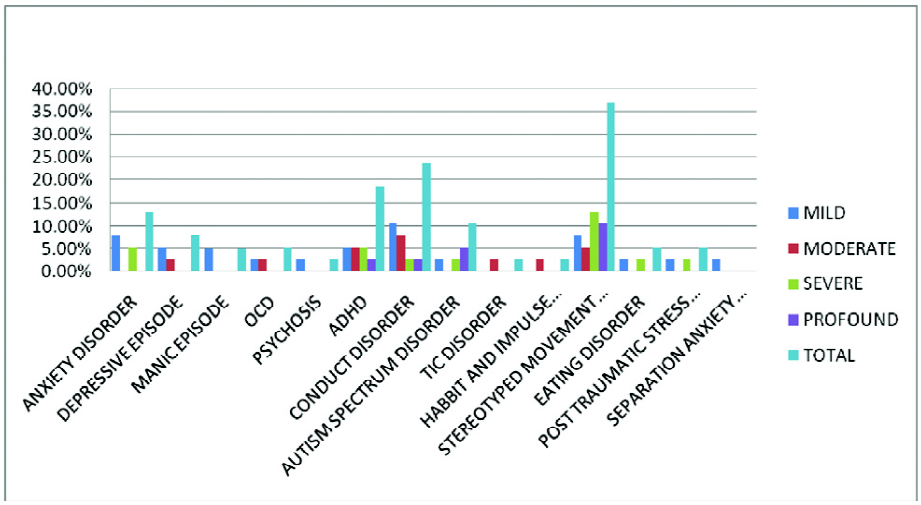


FIGURE 5 : FREQUENCY DISTRIBUTION OF VARIOUS MEDICAL DISORDERS IN DIFFERENT DEGREES OF MR

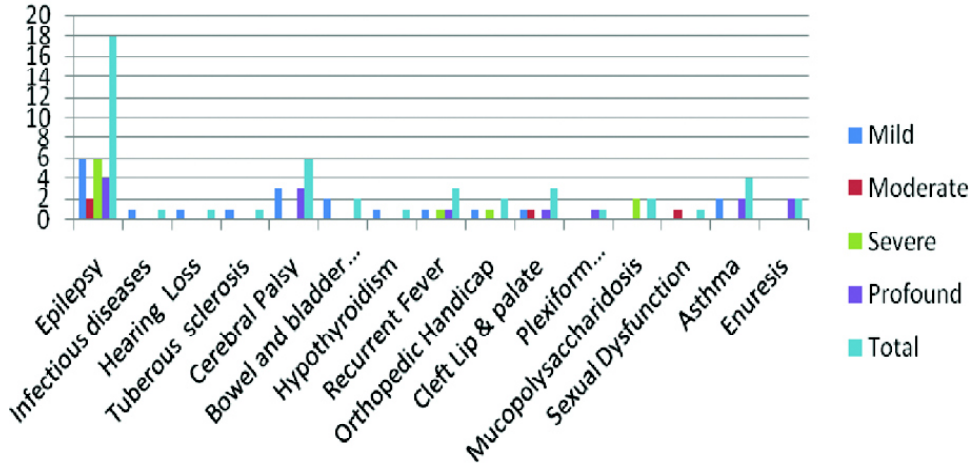


TABLE 3 : FREQUENCY DISTRIBUTION OF VARIOUS PSYCHIATRIC DISORDERS IN DIFFERENT DEGREES OF MR

PSYCHIATRIC COMORBIDITY	MILD	MODERATE	SEVERE	PROFOUND	TOTAL
ANXIETY DISORDER	(3) 7.89%	(0)	(2) 5.26%	(0)	(5) 13.75%
DEPRESSIVE EPISODE	(2) 5.26%	(1) 2.63%	(0)	(0)	(3) 7.89%
MANIC EPISODE	(2) 5%	(0)	(0)	(0)	(2) 5%
OCD	(1) 2.63%	(1) 2.63%	(0)	(0)	(2) 5.26%
PSYCHOSIS	(1) 2.63%	(0)	(0)	(0)	(1) 2.63%
ADHD	(2) 5.26%	(2) 5.26%	(2) 5.26%	(1) 2.63%	(7) 18.41%
CONDUCT DISORDER	(4) 10.5%	(3) 7.89%	(1) 2.63%	(1) 2.63%	(9) 23.65%
AUTISM SPECTRUM DISORDER	(1) 2.63%	(0)	(1) 2.63%	(2) 5.26%	(4) 10.52 %
TIC DISORDER	(0)	(1) 2.63%	(0)	(0)	(1) 2.63%
HABIT AND IMPULSE DISORDERS	(0)	(1) 2.63%	(0)	(0)	(1) 2.63%
STEREOTYPED MOVEMENT DISORDERS (SELF INJURIOUS BEHAVIOUR)	(3) 7.89%	(2) 5.26%	(5) 13.15%	(4) 10.5%	(14) 36.8%
EATING DISORDER	(1) 2.63%	(0)	(1) 2.63%	(0)	(2) 5.26%
POST TRAUMATIC STRESS DISORDER	(1) 2.63%	(0)	(1) 2.63%	(0)	(2) 5.26%
SEPARATION ANXIETY DISORDER	(1) 2.63%	(0)	(0)	(1) 2.63%	(2) 5.26%

TABLE 4 : FREQUENCY DISTRIBUTION OF VARIOUS MEDICAL DISORDERS IN DIFFERENT DEGREES OF MR

MEDICAL COMORBIDITY	MILD	MODERATE	SEVERE	PROFOUND	TOTAL
EPILEPSY	(6) 15%	(2) 5%	(6) 15%	(4) 10%	(18) 45%
INFECTIOUS DISEASES	(1) 2.5%	(0)	(0)	(0)	(1) 2.5%
HEARING IMPAIRMENT	(1) 2.5%	(0)	(0)	(0)	(1) 2.5%
TUBEROUS SCLEROSIS	(1) 2.5%	(0)	(0)	(0)	(1) 2.5%
CEREBRAL PALSY	(3) 7.5%	(0)	(0)	(3) 7.5%	(6) 15%
BOWEL AND BLADDER INCONTINENCE	(2) 5%	(0)	(0)	(0)	(2) 5%
HYPOTHYROIDISM	(1) 2.5%	(0)	(0)	(0)	(1) 2.5%
RECURRENT FEVER	(1) 2.5%	(0)	(1) 2.5%	(1) 2.5%	(3) 7.5%
ORTHOPEDIC HANDICAP	(1) 2.5%	(0)	(1) 2.5%	(0)	(2) 5%
CLEFT LIP & PALATE	(1) 2.5%	(1) 2.5%	(0)	(1) 2.5%	(3) 7.5%
PLEXIFORM NEUROFIBROMATOSIS	(0)	(0)	(0)	(1) 2.5%	(1) 2.5%
MUCOPOLYSACCHARIDOSIS	(0)	(0)	(2) 5%	(0)	(2) 5%
SEXUAL DYSFUNCTION	(0)	(1) 2.5%	(0)	(0)	(1) 2.5%
ASTHMA	(2) 5%	(0)	(0)	(2) 5%	(4) 10%
ENURESIS	(0)	(0)	(0)	(2) 5%	(2) 5%

Discussion

In the present study 60.31% patients had a dual diagnosis, which is similar when compared with other clinical based studies (Philips & Wifiiams, 1975 [9]; Szymanski, 1977[10]; Eaton & Menolascino, 1982[11]). Medical disorders were present in 63.49%, which was found to be more when compared with a study done in children with MR by Khess CRJ etal, 1998 where in a psychiatric disorder was present in 56.17% of the cases, and a medical disease was present in 35.0% of the patients [24]. It was observed that psychiatric co-morbidity was more prevalent in mild to moderate levels of retardation, while opposed to medical co-morbidity which was more prevalent in severe to profound retardation (*P=0.030*). Hence patients with a psychiatric disorder had a milder level of retardation compared to patients with a medical illness. This finding could partly be a reflection of the fact that distinguishing a behavior disturbance from a psychiatric disorder is easier in patients with a milder degree of retardation, hence using operational criteria for diagnosis is more feasible in such cases. On the other hand while dealing with more severely retarded patients, we need to make concessions for diagnostic over shadowing (Riess & Szyszko, 1983)[18]. The other explanation for this could be the fact that patients with medical illness might have suffered from a cerebral damage which was responsible for the retardation as well as the medical illness (like epilepsy), hence the degree of retardation was more in such cases. Malformations and degenerative disorders of the central nervous system are known to be associated with severe neurological abnormalities and cognitive impairment (Bregman & Harris, 1995)[19].

The most common psychiatric disorder found in our study was Stereotyped Movement Disorder, followed by Conduct Disorder and ADHD. This finding was consistent with the views of Lewis and Maclean (1982)[12], who after reviewing the literature, had come to the conclusion that most studies irrespective of the sample and the

methodology, support an increased prevalence of behavioral and emotional disorders. Stereotyped Movement Disorder and Autism Spectrum Disorder were more common in severe to profound MR. Often this is the reason for referral and the focus for psychiatric intervention. Conduct disorder, Psychosis, OCD, Depressive episode, Manic episode and Anxiety disorders were more common in mild to moderate MR. Mood disorders were found to be common in the mild mental retardation . Earlier studies have observed that depression is diagnosed more often in the mildly retarded than in the more severely retarded (Ries et al., 1982, [13]), as the latter may have difficulty in communicating subjective states. Similarly severely retarded manic patients may be lacking in the quality of infectious gaiety and their delusions could be naive (Fraser& Nolan, 1994,[14]). Hence we have to be aware that the clinical presentation may be altered depending on the patient's communicative skills (Szymanski, 1988, [15]).

In this study, 2.63% of the patients were found to have psychosis, which is consistent with previous literature. But a review of previous Indian studies have quoted a higher prevalence rate of 11%, the disparity may be because of not applying the CHA PAS scale specific to MR. [1,4]

ADHD was more commonly associated with mild, moderate and severe MR. Eating Disorders, PTSD and Separation Anxiety Disorders were consistently found in mild MR. Habit and Impulse Disorder and Tic disorder were seen in moderate MR. This frequency distribution was consistent with earlier findings.

63.49% of present sample were diagnosed to have a medical illness of which 52.5% were associated with severe to profound MR. Epilepsy was the most common medical illness, seen in 45% of the patients. Epilepsy had been reported to be common among the retarded, especially the severely retarded (Corbett et al., 1975)[17]. Epilepsy, Cerebral palsy, recurrent fevers, orthopedic handicap, cleft lip and cleft palate, asthma, enuresis and rare syndromes like Mucopolysaccharidosis and plexiform neurofibromatosis were consistently associated with severe to profound MR. Infectious diseases, hearing impairment, tuberous sclerosis, hypothyroidism, bowel and bladder incontinence, sexual dysfunctions were commonly associated with Mild to Moderate MR.

In the present series of patients, psychiatric illness and medical illness were found to coexist in 41.26% of the cases. This is consistent with a biological theory, which presumes that the brain dysfunction that results in mental retardation also predisposes the individual to a mental disorder (Szymanski et al, 1989)[20]. Mucopolysaccharidosis causing retardation and ADHD, Plexiform neurofibromatosis, tuberous sclerosis causing retardation and hyperactivity disorder or autism and epilepsy causing retardation and a wide range of psychopathology are well-recognized facts (Szymanski, 1994)[21].

Conclusion

In conclusion, Psychiatric co-morbidity was more common in mild to moderate mental retardation. Medical co-morbidity was more common in severe to profound mental retardation. Most common psychiatric illness is Stereotyped Movement Disorder, whereas Epilepsy is most common medical illness. Medical illness was more prevalent in severe MR. Psychiatric disorders are commonly diagnosed in milder degrees of retardation as compared to severe retardation, due to diagnostic overshadowing. In such cases, facts like impaired language development behavioral changes, biological changes, family history of mental illness (Sovner, 1989)[22] and the longitudinal history (Tyrer & Shakour, 1990)[23], have to be considered, rather than solely depending on a diagnostic criterion (Szymanski, 1994)[21] or else this could lead to therapeutic nihilism, as we might not make an attempt to treat such cases adequately. In view of the common interface of medical and mental-health problems in mentally retarded, initiatives should be taken to enhance their healthcare following a multidisciplinary approach, laying emphasis on dual diagnosis and diagnostic overshadowing.

Limitations

This was an OPD based study, with a small sample of patients who have come for disability certification that might not have been a true representative of the general population. No specifically designed instrument to assess medical co-morbidity in the retarded was used.

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Orginal Article

Ethmoidal foramina: the rule 24-12-6: is it true for Indian orbits?

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Abstract : Aim : The literature states that the distances between the medial margin of the orbit to the anterior ethmoid foramen, from it to the posterior ethmoid foramen and from it to the optic canal are 24mm, 12mm & 6 mm. This study is to verify if this is true in the Indians as there is no data available in the literature. To the best of our knowledge it is the first study from India, which focused on the relationship of ethmoid foramina. Methods: 70 orbits of 35 Indian skulls were studied, using depth gauge, sliding calipers, dividers and metal scale by a single observer. Results: The average distance between the medial margin of the orbit and the anterior ethmoid foramen is 21.30mm and 20.37mm for right and left orbits respectively (range varying from 18 to 26mm in the right and from 14 to 26 in the left orbit). The average distance between the anterior and posterior ethmoid foramina is 12.45 and 12.47mm (range 6mm to 18mm). The average distance between the posterior ethmoid foramen and the optic canal is 6.32 and 7.37mm (range 2 mm to 18mm). 10 of 35 skulls (28.6%) had 3 foramina instead of 2 (accessory foramen), involving right orbit in 5, left in 4 and both the orbits of a skull. Conclusions: The rule 24-12-6 does not apply to Indian orbits. The anterior Ethmoid foramen is about 3mm nearer to the orbital margin. There is a great variation in the distances of ethmoid foramina. Nearly a third of the skulls have accessory ethmoid foramen.

Key Words : Rule of 24-12-6, Anterior Ethmoid foramen, Posterior Ethmoid foramen, Optic canal, Accessory foramen,

Introduction

The relationship between the ethmoid foramina and the optic nerve is interesting as the conventional literature[1, 2]. States that the distances between the medial margin of the orbit to the anterior ethmoid foramen (AEF), from it to the posterior ethmoid foramen (PEF) and from it to the optic canal (OC) are 24mm, 12mm & 6 mm respectively while differences in this anatomical relationship of the bony orbit depending on the race were described[1, 3, 4, 5, 6]. Some studies[7, 8] showed the presence of accessory foramina. Accessory foramina upto 6 in number, in an orbit was also cited[8]. These studies were made on dry skulls or from imaging[9]. There is only one article in the literature available regarding anthropometric studies of bony orbit among Indians[10]. Hence, a study was conducted to examine the distances between the ethmoidal foramina, presence of any accessory foramina, and verify if the 24-12-6 rule is true in the Indian skulls, since a knowledge of it will be of use not only for orbital surgical approaches but also for other approaches[11].

Meterials and Methods

Seventy orbits of thirty-five Indian skulls available at the department of Anatomy, of Maharajah's Institute of Medical Sciences, were studied. The most anterior and the most prominent posterior ethmoidal foramina were identified as the anterior and posterior ethmoidal foramina (Fig.1) and all others as the accessory foramina. The distances from medial orbital margin to AEF, from it to PEF and PEF to OC were measured'. When accessory foramen was noted, its distance to PEF and OC are measured. Vernier calipers, sliding-calipers, surgical calipers, depth gauge, compass and scale were used to record these measurements, which were taken by a single observer to prevent inter-observer variation.

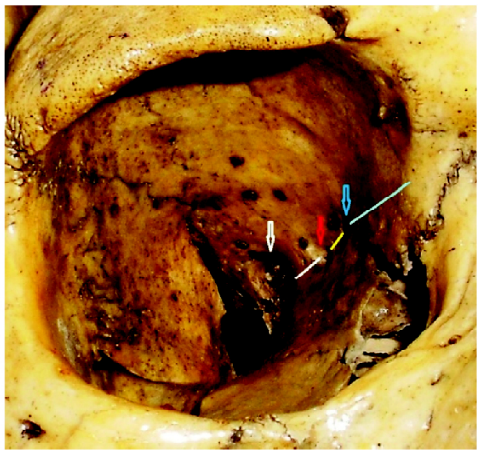

Fig 1: Foramina and distances between them: Blue arrow points towards anterior ethmoidal foramen ;red arrow points towards posterior ethmoidal foramen; white arrow points towards optic foramen; blue line shows distance between medial orbital margin to anterior ethmoidal foramen; yellow line shows distance between anterior to posterior ethmoidal foramina; white line shows distance between posterior ethmoidal foramen to optic foramen

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Results

The measurements between the orbital margins, AEF, PEF, OC, Accessory foramen are tabulated (Table 1) from which meaningful conclusions could be drawn. We can see lot of variations in the measurements among the orbits. We can also observe gross asymmetry between the right and left orbits.

TABLE 1: Distances between orbital margin, EF, PEF and Accessory Foramina and the Optic Canal

RIGHT ORBIT				LEFT ORBIT			
AEF to Medial orbital margin	AEF to PEF	PEF to Optic foramen	PEF to Accessory foramen	AEF to Medial orbital margin	AEF to PEF	PEF to Optic foramen	PEF to Accessory foramen
24	10	5		23	10	7	
20	8	7		18	6	5	5
22	11	4		20	15	6	
21	8	9	9	20	18	5	3
18	16	4		20	12	3	
26	14	10		22	11	2	
20	9	12		28	15	16	
19	13	6		23	9	8	
21	16	8		23	15	10	
26	12	8		17	16	8	
24	11	3	5	17	8	10	12
23	12	6		19	10	18	
24	8	6		20	12	9	
21	10	10		20	11	6	
20	9	3	7	20	16	9	
22	13	9		21	9	10	
22	17	4		22	12	8	
20	16	4		20	18	7	
18	10	6	4	21	15	7	
18	15	5		21	11	5	
18	14	6		21	12	4	
20	2	6	6	22	12	7	
28	12	6		22	12	4	
19	14	4		25	15	6	
20	16	3		20	15	2	
19	16	5		18	15	9	
20	19	6		21	7	5	
23	12	5		20	16	4	
23	11	5	8	23	13	3	
18	14	6		23	10	3	10

The average distance between the medial margin of the orbit and the anterior ethmoid foramen is 21.30mm and 20.37mm for right and left orbits respectively (Table 1). The range was varying from 18mm as the shortest and 26mm as the longest distance (Fig.2) in the right orbit and from 14mm as the shortest (Fig.3) and 26mm as the longest distance in the left orbit (Table 2).

Fig 2: Blue line shows longest distance between medial orbital margin and anterior ethmoidal foramen (26mm)

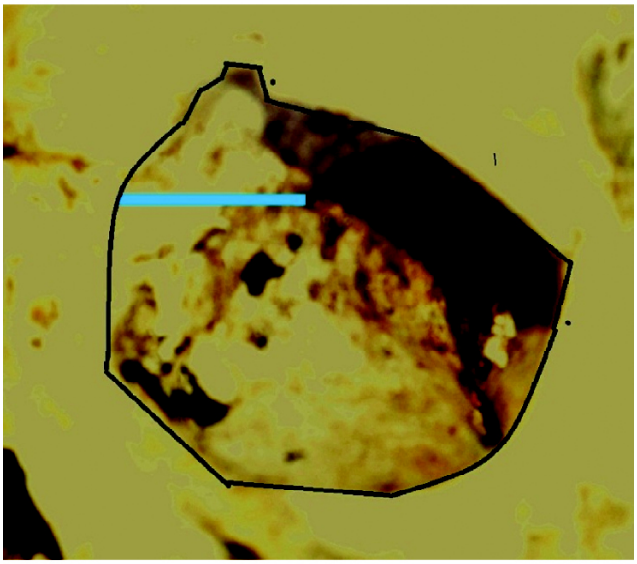

Fig 3: Blue line shows shortest distance between medial orbital margin and anterior ethmoidal foramen(14mm)

The average distance between the anterior and posterior ethmoidal foramina is 12.45 mm and 12.47mm for the right and left orbits respectively (Table 1). The shortest distance between the two foramina was found to be 2mm (Fig.4) and the longest distance18mm (Fig.5) in both the right and left orbits (Table 2)

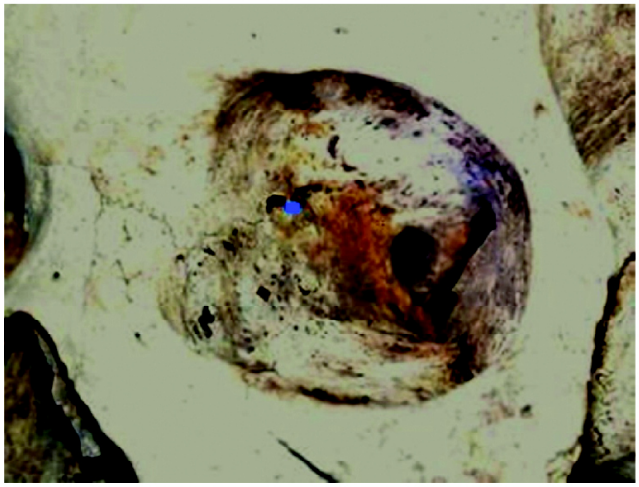

Fig.5 : Blue line shows shortest ethmoidal anterior to posterior foramina (2 mm)

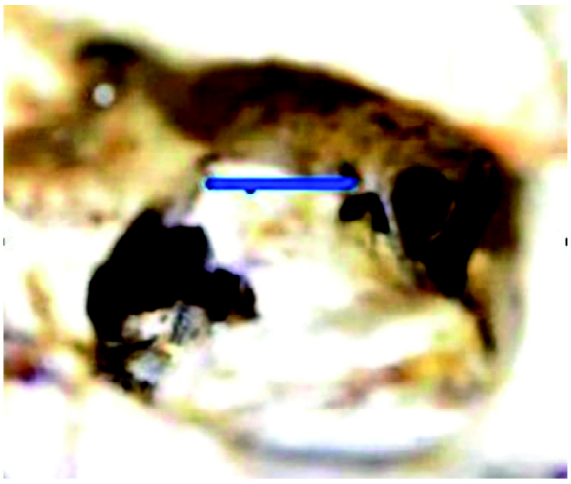

Fig.5 : Blue line shows longest ethmoidal anterior to posterior foramina (18 mm)

The average distance between the posterior ethmoidal foramen and the optic canal is 6.32in the right orbit and 7.37mm in the left orbit (Table 1) with distances varying from as short as 2mm and as long as 18mm in both right and left orbits. (Table 2) There are 10 orbits which showed accessory foramen (3 instead of 2). (Fig.6a and 6b). The accessory foramen was present in 5 right orbits, 4 left orbits and 1 was present bilaterally (Table 3).

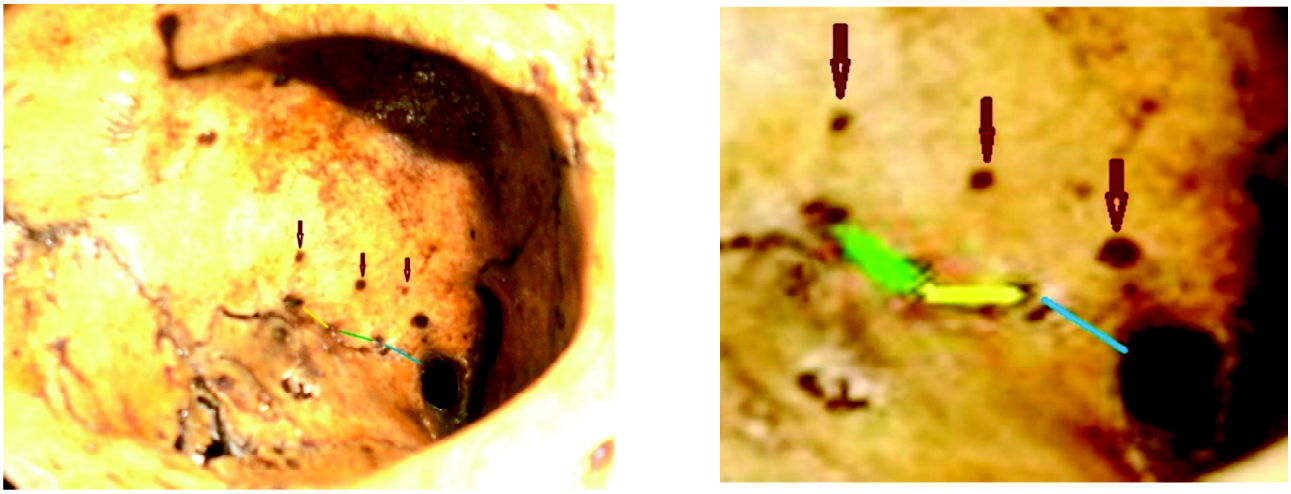

Fig.6 a: 1-anterior ethmoidal foramen ; 2-posterior ethmoidal foramen; 3-accessory foramen; 4-optic foramen; yellow line represents distance between anterior to accessory foramen; green line represents distance between accessory foramen to posterior ethmoidal foramen; blue line represents distance between posterior ethmoidal foramen to optic foramen; 6b-foramina in detail

Table 2: Longest and shortest distances between the foramina

	RIGHT ORBIT			LEFT ORBIT		
	AEF to medial orbital margin	AEF to PEF	PEF to optic foramen	AEF to medial orbital margin	AEF to PEF	PEF to optic foramen
Longest	26	18	18	26	18	18
Shortest	18	2	2	14	2	2

Table 3: presence of accessory foramina in the right and left orbits

RIGHT ORBITS	LEFT ORBITS	BILATERAL
5	4	1

Maria Piagkou studied 249 dry orbits and assessed that the distances between anterior lacrimal crest (ALC) to AEF, AEF-PEF, and PEF to optic canal (OC) in Greek population was "23-10-4 mm". A variation in the number of ethmoidal foramina was found, ranging from 1 to 6. A significant gender difference was observed for ALC-AEF in males (20.67-26.39) versus females (18.79- 26.23). [8](Tables 4 and 5)

Abed SF studied 47 orbits and analyzed that the average distances from the anterior lacrimal crest to AEF, PEF and OC were 25.61 mm, 36.09 mm, and 43.77 mm. The average distance between the AEF to first PEF, last PEF, and optic canal were 13.88mm, 16.60 mm and 21.65 mm respectively. The average distances from the first and last PEF to the optic canal were 11.63mm and 7.25 mm respectively. They found that the distance between the PEF to the OC is more than double the distance quoted in the surgical literature[4]. (Table 4)

Takahashi studied 54 orbits and found from them that the mean distances from anterior lacrimal crest to anterior and posterior ethmoidal foramina and the optic canal were 19.6 mm, 33.5mm, and 41.9 mm respectively[7]. In another study among 84 orbits, he found accessory ethmoidal foramina in 32 orbits, one accessory foramen was identified in 30 orbits, and 2 foramina in 2 orbits[3] (Tables 4 and 5).

In a study which was conducted by Ashwini Mutalik, the distance between the AEF to PEF ranged from 3-18mm and the distance between PEF to optic canal ranged between 2-18 mm[10].

In a study conducted by Huanmanop in Thai subjects, the mean distances from the anterior lacrimal crest to the optic canal, anterior, and posterior ethmoidal foramina were 42.2, 23.5, and 36 mm for both sides and genders, respectively[5].

In a study by Pereira and Lopes, 38.67% of accessory ethmoidal foramina were present on right side and 48.38% were on the left side[6]. Accessory foramina were less in number in males than in females.

Table 4: Distances between foramina in various races

Studies	Distance between medial orbital margin to AEF	Distance between AEF to PEF	Distance between PEF to Optic foramen
Present study	20.83	12.46	6.84
Greeks[8]	23	10	4
Caucasians[4]	25.6	13.88	11.6
Chinese[7]	19.6	13.9	8.4

The relationship of anterior and posterior Ethmoid foramina to the orbital rim and the Optic canal has shown significant difference among different races. Knowledge of these changes is of importance in this era of frequent migration of doctors and patients.

Table 5: Presence of accessory foramina among various races

Studies	Number of orbits with accessory foramina	Number of orbits with Single accessory foramen	Extra foramina	Orbits with Bilaterally present accessory foramina	Number of orbits studied
Present study	10	9		2	70
Greeks[8]	22	15	5 EF in 2 orbits6 EF in 1 orbit		249
Chinese[3]	32	30	2 EF in 2 orbits		84

Conclusion

This is the first study on the rule of 24-12-6 among Indians' orbits. Rather than the 24-12-6 rule, 21-12-7 rule applies to the Indian skulls. Therefore, it is important for the orbital and ENT surgeons to know about this variation. This knowledge is helpful during surgeries involving the medial orbital walls, both for the orbital surgeon and the ENT colleague. The presence of accessory ethmoid foramen in nearly 30% of Indian skulls is to be known and remembered by these surgeons.

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Original Article

Prospective Study of Peripheral Nerve Tumors over a period of 2 Years

Suryakala Chappa, Sudhasmita Rout, K Prasad Reddy, PVB Ramalakshmi

Abstract : Peripheral nerve tumors arise from Schwann cells and perineural cells. Most of them are benign but have overlapping entities with different course of prognosis, recurrence and malignant transformation. The practicing pathologist must be familiar with their morphological features. We report 22 cases of Neural tumors, of which 11 were Neurofibromas, 10 were Schwannomas and 1 was Malignant Peripheral Nerve Sheath Tumor (MPNST).

Key Words : Neurofibroma, Peripheral nerve tumors, Schwannoma

Introduction

Peripheral nerve tumors arise from Schwann cells, Perineurial cells and Fibroblasts. Majority of them are benign but they have overlapping entities, different course of prognosis, recurrences and malignant transformation. The practicing pathologist must be familiar with their morphological features. An inherent challenge to the FNAC evaluation is that, there is cyto-morphological overlap between benign and malignant lesions. With FNAC, there is dispersion of individual cells and partial loss of recognizable tissue pattern, leading to less specific diagnosis. Our aim is to prove the efficacy of FNAC in the diagnosis of peripheral nerve tumors and its histological correlation.

Aims and Objectives

To identify the age, sex and site wise distribution of neural tumors, identify type of neural tumor and to correlate cytology with histopathology.

Materials and Methods

The present study is a prospective study of neural tumors conducted at the department of pathology, Maharajah's Institute of Medical Sciences, from Jan 2012 to Dec 2013. All patients of peripheral nerve tumors were subjected to FNAC followed by biopsy. Aspiration was done with 22G needle and 5cc syringe and smears stained with Hematoxylin-Eosin(H&E). For histopathology, the tissue was formalin fixed and paraffin embedded sections were cut and stained with H&E. Special stains and immuno-histochemistry (IHC) were done wherever necessary.

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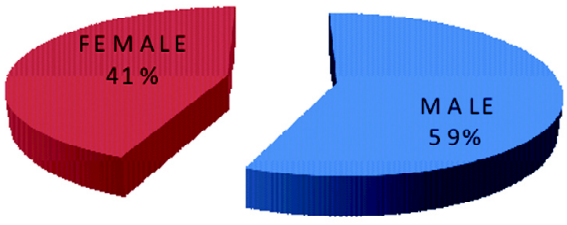
Results

Out of 167 cases of soft tissue tumors, 22 were peripheral nerve tumors. Among these 22 cases of peripheral nerve tumors 21 were benign and 1 was malignant. On FNAC all cases were reported as benign and on histopathology, 1 case was malignant.

Age Distribution

Parameter	Age (years)
Mean Age	38
Youngest age	11
Oldest age	76

Sex Distribution



Site Distribution

Site distribution	Number of cases
Head & neck	08
Lower extremity	07
Upper extremity	06
Trunk	01
Total	22

Types of Peripheral nerve tumors number

Neurofibromas	11
Schwannomas	10
MPNST	01
Total	22

Cyto-Histological Correlation

Cytology: Benign: 22, Malignant: 0.

Histopathology: Benign: 21, Malignant:1

Correlation = 95.45%

Discussion

Peripheral nerve tumors are classified into:

1) Benign: Schwannoma, Neurofibroma, Perineurioma
2) Malignant: MPNST (Malignant Peripheral Nerve Sheath Tumors)
3) Non-neoplastic: Traumatic neuroma and Morton's neuroma[1]

Schwannoma (Neurilemmoma) : Encapsulated tumor with yellowish cut surface with cystic degeneration(fig1). Mostly solitary but multiple and bilateral tumors can occur in association with NF2. Most common sites are head & neck, flexor aspects of upper and lower limbs. Other sites are mediastinum, retroperitoneum and cerebello-pontine angle.

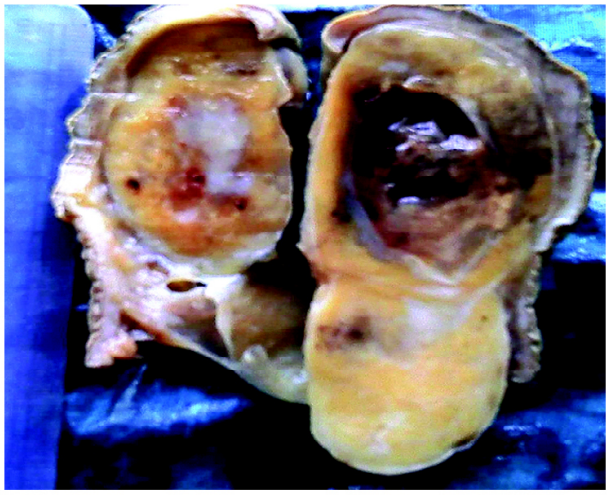


Fig 1. Schwannoma - gross. Note the well encapsulated tumor with yellowish discoloration and cystic changes

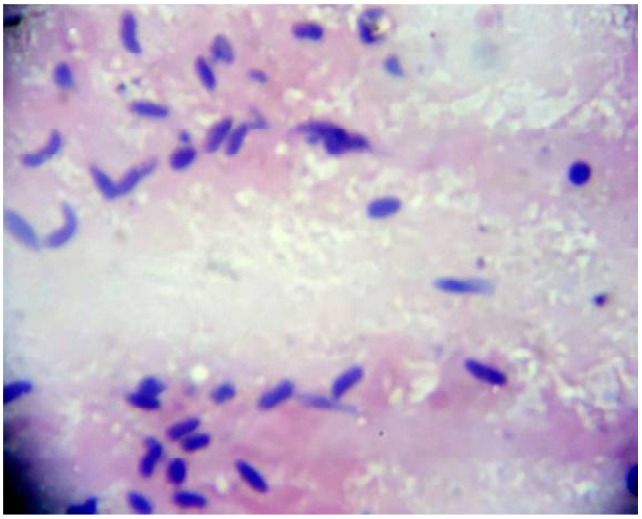


Fig 2. FNAC showing hypo-cellular smears with benign spindle cells

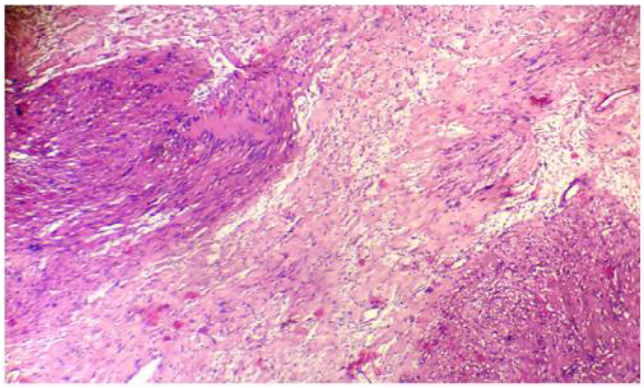


Fig 3. Schwannoma histopathology showing Antoni A and Antoni B areas

FNAC shows benign spindle cells and the smears are hypo-cellular (fig.2). Microscopy hallmark is the pattern of alternating Antoni A and B areas (fig3). Malignant transformation in Schwannoma is a very rare event unlike in neurofibromas. A rare variant of psammomatous melanotic Schwannoma is regarded as low grade malignancy because of its tendency for local recurrence.

Neurofibroma : Classified into

1) Localised: not associated with genetic syndromes
2) Diffuse: most common in head & neck as raised plaque lesion.
3) Plexiform: entire length of nerve is involved to appear as a bag of worms.

Diffuse and plexiform neurofibromas are associated with NF1.

Grossly appears as well-circumscribed, with cut surface yellowish and mucoid (fig4). Microscopy shows interlacing bundles of elongated cells with wavy dark nuclei (Fig5).

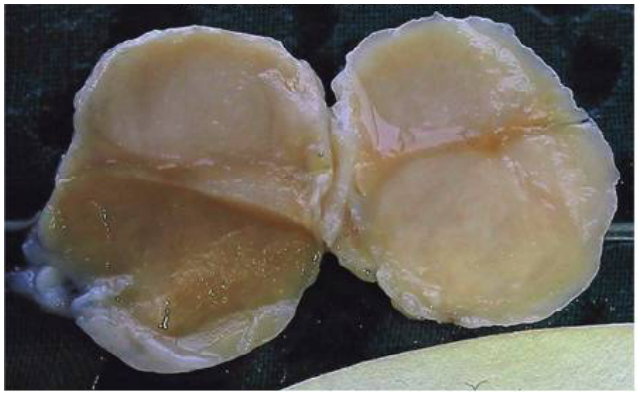


Fig 4. Neurofibroma – Gross well circumscribed yellowish white mucoid cut surface

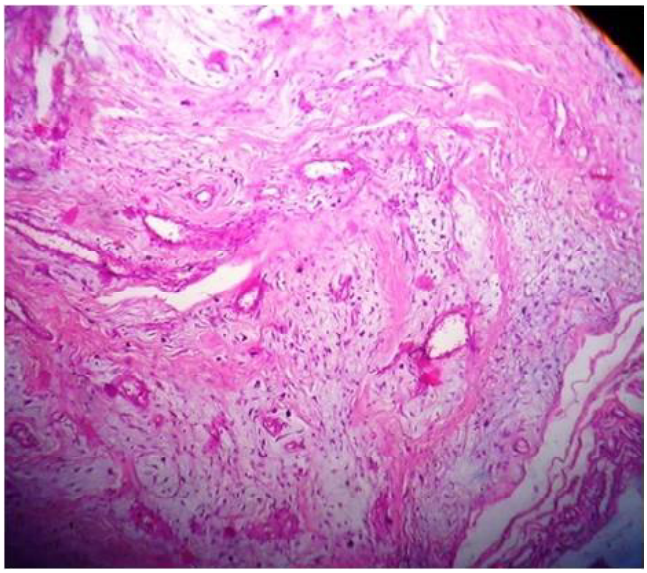


Fig 5. Histopatholgy neurofibroma showing Schwann cells, Fibroblasts and Nerve bundles

Neurofibromatosis (Von Recklinghausen disease)

Autosomal dominant. Type1 : NF1 gene is located on chromosome 17. It presents as plexiform neurofibromas (elephantiasis neuromatosa) with café-u-lait spots and Lisch nodules on the iris. Other associated features include megacolon, schwannomas, pheochromocytoma, neuroblastoma and GIST. Type2 : associated gene is NF2 is located on chromosome 22. It presents in CNS tumors like bilateral acoustic schwannomas, meningiomas, Optic nerve gliomas and astrocytomas. MPNST : Arise de-novo or part of Type 1 von Recklinghausens disease.

Neurofibromatosis should be suspected if tumor develops in Type 1 NF or tumor arising within the anatomic site of a major nerve. Grossly it is a large fusiform mass, fleshy, opaque, white-tan surface marked by areas of secondary hemorrhage and necrosis (fig6). Microscopy shows densely cellular fascicles alternate with hypocellular, myxoid zones, creating a marble-like effect (fig7). IHC of peripheral nerve tumors shows S-100 positivity (fig8).

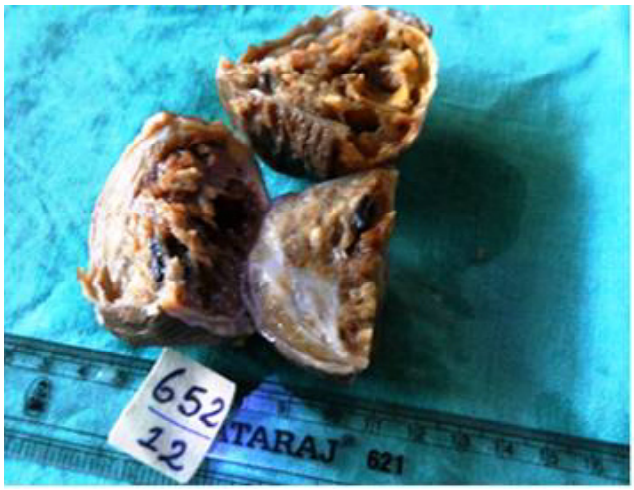


Fig 6. MPNST Gross section showing yellowish white masses with haemorrhage and necrosis

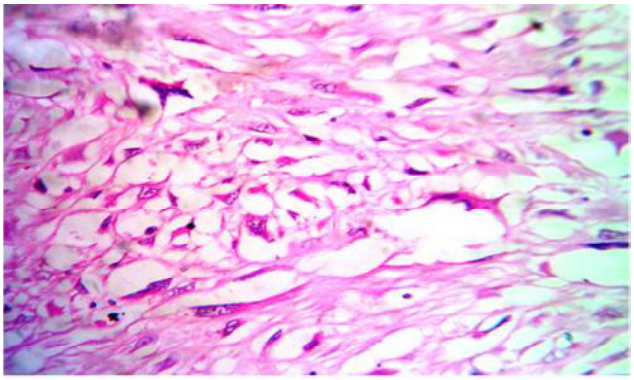


Fig 7. MPNST microscopy showing cellular areas with bizzare hyperchromatic nuclei

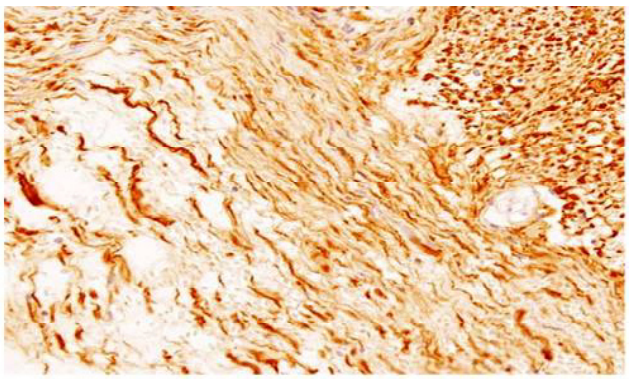


Fig 8. IHC for Schwannoma, S100 strong positivity

Conclusion

Most peripheral nerve sheath tumors in this study were benign. The mean age of patients was 36 years. The most common site was head and neck. Fine needle aspiration provided a relatively non-traumatic rapid diagnosis. Benign tumors ware easily diagnosed by FNAC, but benign cellular tumors and low grade malignancies needed confirmation by histopathology. The present study, whose aim was to prove the efficacy of FNAC as a useful tool and a reliable technique in diagnosing peripheral nerve tumors showed a sensitivity of 100% and specificity of 95.5%.

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Case Report

Endoscopic Calcaneoplasty for Haglund's deformity

S.Appala Raju[1], M Vijay Bhushanam, G Rajasekhar Rao, M Venkateswara Rao

Abstract : Endoscopic calcaneoplasty is a minimally invasive technique for resection of inflamed retrocalcaneal bursa and resection of abnormal prominence over the postero superior part of calcaneum.In this report, we describe the treatment of Haglund's deformity by minimally invasive method to overcome wound healing problems.It also offers an advantage of shorter recovery time and proved cosmesis

Key Words : Haglund's deformity, calcaneoplasty, endoscopic surgery,

Introduction

In 1928, Swedish orthopedic surgeon Patrick Haglund described a patient with a painful hindfoot caused by a prominent posterosuperior aspect of the calcaneus in conjunction with a sharp rigid heel counter[1]. The term Haglund's disease, deformity and syndrome are used interchangeably.

Haglund's disease is defined as a complex of symptoms involving the superolateral calcaneal prominence, retrocalcaneal bursitis and adventitious Achilles tendon bursitis[2, 3, 4]. On physical examination, a bony prominence can be palpated at this location. This entity is described by a variety of different names such as 'pump-bump'[5], 'cucumber heel'[6], 'high-prow heels'[7] and 'winter heel'[6] Non-surgical treatment is always recommended first. If pain persists with conservative treatment and a bony exostosis is confirmed by imaging, surgery is considered. The conventional surgical treatment is an open resection [3,4]Recently, several authors reported good results with an endoscopic technique[4, 8, 9, 10, 11]

Case History Mrs K M , female 38 yrs of age, has presented to the outpatient department of orthopaedics, Maharajah's Institute of Medical Sciences with complaints of pain in the left heel since 2 years for which she underwent conservative management with non-steroidal anti-inflammatory medications and physiotherapy without any relief. Clinical examination showed swelling and tenderness over the posterosuperior part of left heel (figure 1).

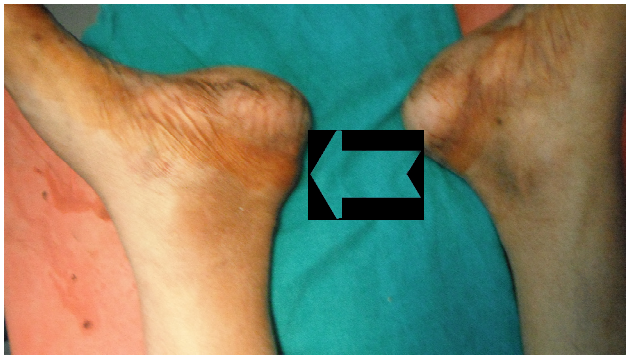

Fig 1 clinical photograph showing left sided heel bump (red arrow)

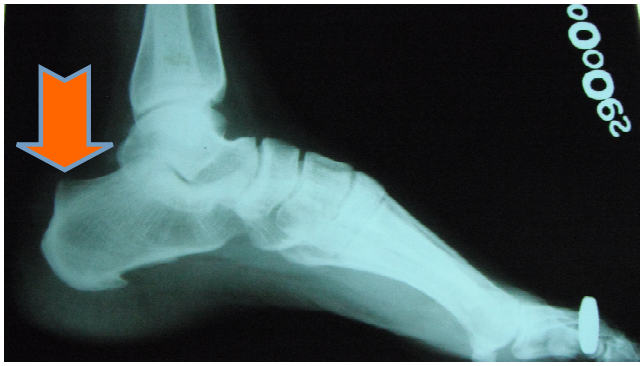

Figure 2 : Pre-op x-ray showing bony overgrowth

X-Ray of the foot showed postero-superior bony bump, suggestive of Haglund's deformity (figure2).

Surgical technique : The patient was operated under general anaesthesia with tourniquet control over the thigh. The patient was placed in prone position with the ankle hanging freely over the edge of the operating table to allow full range of movement during the procedure. A support is placed below the leg for maneuverability with instruments (figure3).

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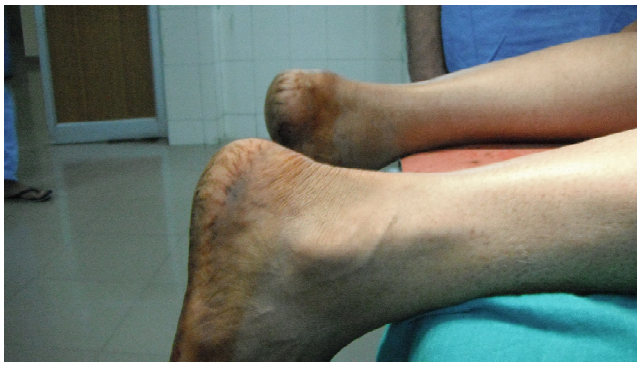

Figure 3 position on operation table

Two portals were placed adjacent to the Achilles tendon on either side. Initially a 4-mm scope is placed through the lateral portal. With a 4-mm synovial resector the soft tissue was debrided through the medial portal on the bone side and tendon side. The Achilles tendon was protected throughout the procedure by keeping the closed end of the shaver against the tendon .The bone was resected with a mastoid burr. Both the resector and scope were interchangeably used through both the portals. After resection, the Achilles tendon was inspected through scope and confirmed to be intact. At the end of the surgery, Plantarflexion of ankle was found to be satisfactory by squeeze test. Portals were closed with 2-0 ethilon (figure4)

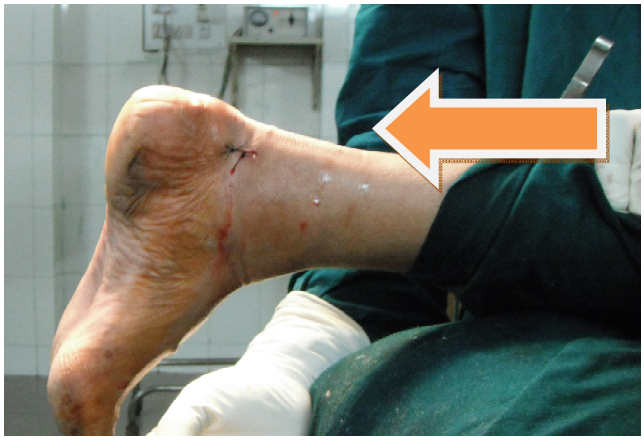

Figure 4 showing arthroscopic closure

Wound was dressed and a compression bandage was applied.

Post operative management: Post operative period was uneventful. Patient received volar slab upto below knee extent with ankle in plantarflexion . The patient was trained for nonweight bearing mobilization till 2 weeks, and later changed to neutral position of ankle and was trained for weight bearing. By 6 weeks she returned to normal activity. X-ray showed good clearance for Achilles tendon and removal of bony swelling (Figure 5 and 6)

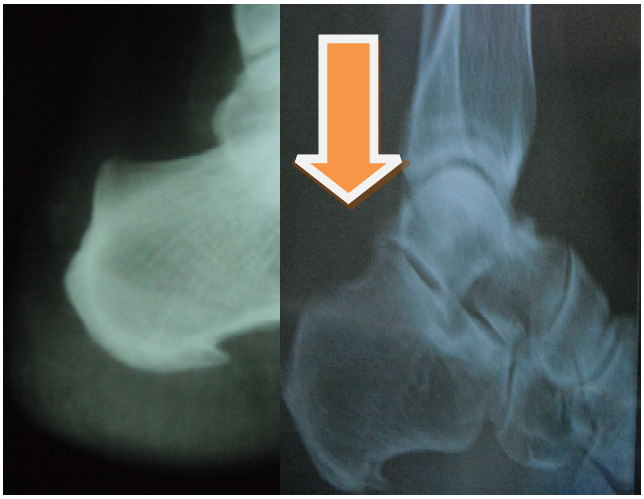

Figure 5 (left) Pre-operative x-ray showing Haglund bump and figure 6 (right) showing Post-op x-ray with removed bony bump shown by arrow head

Using the Oglive-Harris[12] score after 6 months she had excellent results (AOFAS score 98).

Discussion

In summary, whether the operation is performed by endoscopic or open surgery, enough bone has to be removed to prevent impingement between the calcaneus and Achilles tendon. The endoscopic calcaneoplasty is an excellent alternative to the open method, as it has several advantages like low morbidity, excellent scar healing, a short recovery time and quick resumption to normal activities including sports. The functional recovery is excellent and compares favourably to open method. Thus endoscopic calcaneoplasty has a definite role in the management of Haglund's deformity.

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Conflict of Interest : Declared None

Case Report

Role of Neuro-Imaging in Dengue Encephalitis

Madhavi C[1], GS Kejriwal[2], Giridhar Gopal G[3]

Abstract : Dengue infection is endemic in many tropical countries and its incidence is increasing worldwide. The important neurological complications are encephalopathy and encephalitis , the former being more common. Along with serological and CSF examinations, imaging with CT or MRI is important to look for structural changes in brain and if present, to define the pattern and extent of involvement of brain parenchyma. Here we report 2 cases of a children with serologically proven dengue fever having features of dengue encephalitis on imaging. This report is to emphasize the role of imaging in dengue fever with neurological manifestations.

Key Words : Bilateral thalamic hypodensity, CT scan, Dengue fever, Encephalitis, Neurological involvement

Introduction

Dengue viruses are single stranded viruses of Flaviviridae family, which can cause dengue fever and dengue hemorrhagic fever. A myriad of systemic manifestations can occur and the neurological manifestations play a great role in increasing the mortality and morbidity. The role of imaging has become indispensable to evaluate the structural changes in brain and thereby assessing the prognosis of the patient.

Case Report

Case 1 A boy, 10 yrs of age came to the emergency department with complaints of high-grade fever for 7 days, seizures for 3 days and altered sensorium for 2 day, There was no evidence of any muco-cutaneous rash or haemorrhagic manifestations.

The patient was admitted in pediatric intensive care unit. On examination, there was hypertonia involving all 4 limbs, brisk reflexes, plantar extensor & ankle clonus. His Glasgow Coma Scale was '6' at admission. Laboratory examinations revealed a platelet count of 1.4 lakhs and serum was positive for IgM and IgG dengue antibodies and negative for Malarial parasite, Hepatitis A, B, C and Japanese encephalitis virus. CSF examination showed evidence of dengue antigen, protein 8.4mg/dl, sugar 60mg/dl and differential count showing 100% lymphocytes.

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Patient developed involuntary movements during second week of stay in hospital and imaging of brain was performed. MRI brain was attempted but abandoned as sedation failed. Hence plain & contrast CT scan was taken. On plain CT, there were areas of multiple focal hypodensities in parietal lobes, right frontal lobe and in both cerebellar hemispheres. Hypodensities were also noted involving bilateral thalami with foci of hyperattenuation within, suggesting hemorrhage (Fig1&2). Pons & midbrain were mildly expanded with diffuse hypodensity (Fig3). Cortical sulci are diffusely effaced with mild compression of lateral ventricles, suggesting diffuse cerebral edema (Fig4).

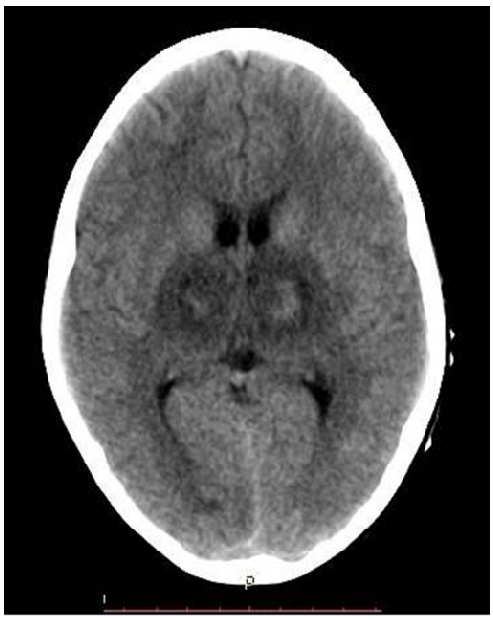

Fig 1: NECT brain showing bilateral thalamic hypodensity with small foci of hemorrhagic attenuation

The diagnosis of encephalitis was made and with conservative treatment he recovered slowly. After 40 days he was discharged. On follow-up 3weeks later, he has regained near normal tone of limbs with only persistence of involuntary movements to some extent.

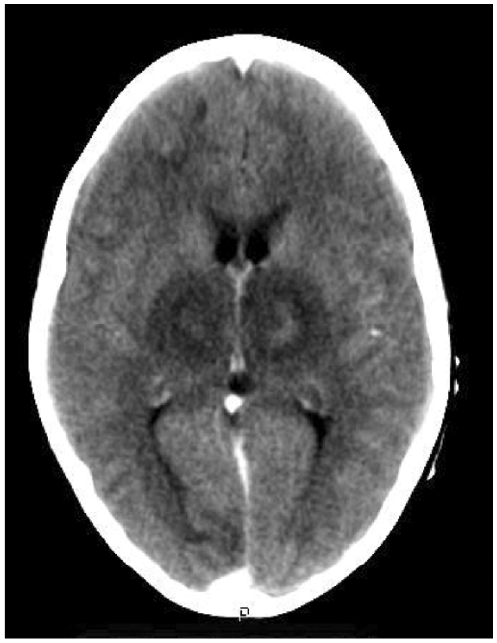

Figure 2: CECT brain showing no enhancement of bilateral thalamic hypodensity and central area of hemorrhagic attenuation.

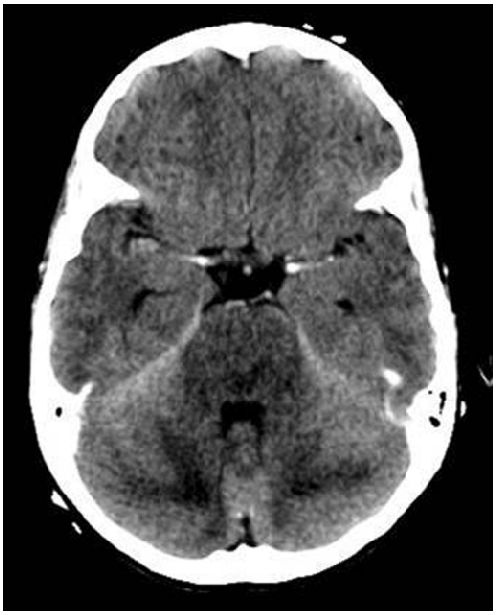

Figure 3: CECT brain showing non enhancing hypodensity with mild expansion of pons and symmetrical hypodensities in both cerebellar hemispheres

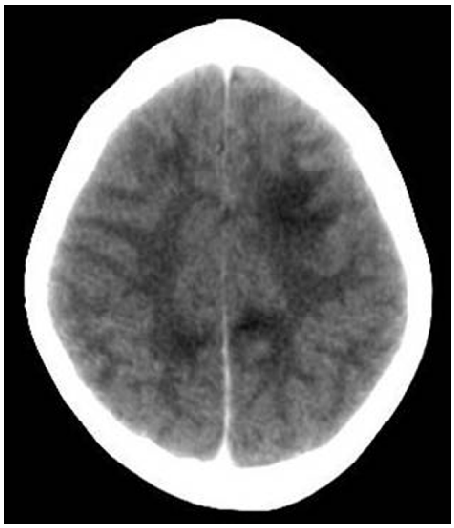

Figure 4: CECT brain showing non enhancing hypodense areas in both high parietal lobes

Case 2 : Another boy, 5 Years of age attended the outpatient department of paediatrics with complaints of high grade fever of 4 days duration. There was no history of respiratory, gastro-intestinal or neurological symptoms, Examination revealed mild hepato-splenomegaly. His TLC was3,100/cmm DC N 65, L 25,E 5 and platelets 81,000/ cmm. He was tested negative for Malaria Parasite and Positive for Dengue IgM and IgG antibodies.

His CT scan showed ill defined hypodensities in both the Thalami and pons , resulting in mild expansion(Fig.5)

Within few hours of admission the child developed hematemesis and seizures with tonic posturing of limbs. His platelet count dropped to 10,000/cmm within a span of 6 hours. Despite aggressive management including platelet infusion and ventilator assistance, the child expired on the second day.

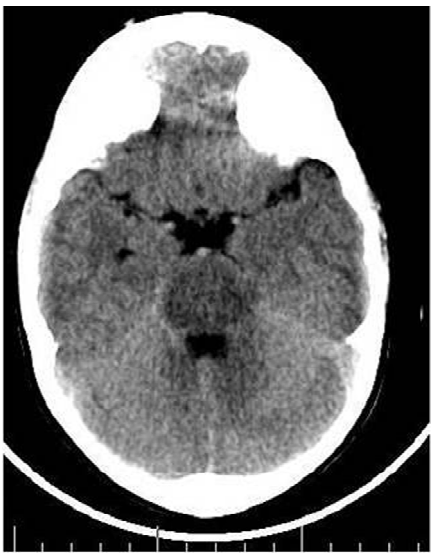

Fig 5: Plain CT brain showing ill-defined hypodensity with mild expansion of pons

Discussion

Dengue viruses are single stranded viruses of Flaviviridae family, which can cause dengue fever and dengue hemorrhagic fever. The involvement of brain in dengue fever can occur either in the form of encephalopathy or encephalitis. Encephalopathy is more common and may occur with multi-system derangement like hepatic failure, shock, coagulopathy and bacterial infections. As the pathogenesis implies, the changes in brain on imaging are seen diffusely, with no particular focal lesion. On the other hand, Encephalitis occurs due to inflammation of brain tissue due to direct virus infection[1]. Although it was previously thought that dengue virus was non-neurotropic, recently there is increasing evidence of neurotropic nature of virus as the virus was isolated from CSF [2]. The other neurological complications of dengue infection are meningitis, myositis, myelitis, stroke, hypokalemic paralysis, post infection sequelae like acute disseminated encephalomyelitis, neuromyelitis optica, optic neuritis, Guillian-Barre syndrome etc[3].

On imaging in our case of encephalitis, CT and MRI depict the multiple focal lesions in cerebral parenchyma, cerebellum, and brainstem along with the bilateral thalamic involvement. This pattern of brain involvement was classically described in case of Japanese encephalitis[4] However, now there are case reports with similar brain lesions in case of dengue encephalitis too[5] Bilateral thalamic involvement with evidence of hemorrhage in dengue fever, similar to our case has been described by Kapil B.et al[6]. The list of differential diagnosis with this kind of bilateral thalamic lesions includes Flavivirus infection, Bilateral thalamic glioma, Wilson's disease, hypoxia, Osmotic myelinolysis, Cerebral arterial and deep vein thrombosis, Creutzfeldt-Jacob disease and Leigh's disease.

Conclusion

Whenever a patient with serologically proven dengue infection is encountered with features of encephalopathy, the possibility of encephalitis has to be considered and prompt imaging should be carried out. Imaging is of utmost value to confirm or rule out the presence of encephalitis, to rule out the other differential diagnoses and in the follow-up of the critically ill patient. MRI is the most sensitive modality and the imaging method of choice as it can provide better visualization of brain substance and superior in displaying the posterior fossa structures. However, the role of CT is indispensable in case of non co-operative and sick patients, in whom the study cannot be conducted for long time, and in remote areas, where MRI is not available.

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Original Article

Unusual Huge Rectosigmoid Foreign Body

P Syama Prasad, Raj kumar, Himaja

Abstract : Anorectal foreign bodies are mostly due to insertion through anus. Rarely they reach the rectum via the oral route. They are usually inserted for sexual[1] or medical (diagnostic or therapeutic) purposes or could be due to child abuse or criminal assault[2]. Cylindrical objects are more common since they can be easily inserted. They can cause ano-rectal trauma and rarely serious complications like perforation. Removal of large foreign bodies often requires surgery. Here we present a rare case of accidental trans-anal introduction of a huge foreign body (beer bottle) into the rectum.

Key Words : Rectal foreign body, Perforation, Anorectal trauma

Introduction

Large Foreign Bodies in recto-sigmoid are uncommon. Objects can be inserted for medical purpose as diagnostic tools or therapeutic purpose or self treatment of ano-rectal diseases eg prostatic enlargement, removal of impacted faeces[2], accidental break of thermometer while recording rectal temperature.[3]. Few cases in the literature described foreign bodies in the rectum in association with Munchausen's syndrome in psychiatry patients[4,5].

A wide variety of foreign bodies in rectum were documented that were used for erotic activity such as dildos or vibrators. In the literature many common as well as exotic objects which have been inserted through the anus, were recorded, which included light bulbs, candles, shot glasses, unusually large objects such as soda or beer bottles[6]. Objects to conceal include drug packets, weapons, guns and knives.

These patients commonly present with pain, discomfort or foreign body sensation. They present to the doctor after their attempts to remove the object fail[7]. Social embarrassment and stigmas hinder the patient to seek immediate medical care. Patients may come up with unusual stories to explain how the object was lodged in the rectum.

Case Report

Mr. M.R, a male, 32 years of age, a vegetable vender, presented with the complaints of colicky abdominal pain and mass per abdomen of 12 hours duration following sitting on a beer bottle after consuming beer. There was no history of vomiting, diarrhea, fever or bleeding per rectum. General and systemic examinations were essentially normal. On examination a vertically oval mass, 16×8 inches in size, with well defined borders, was seen in the epigastric and umbilical regions of abdomen (fig.1). It was hard in consistency. There was no organomegaly. It was dull on percussion, and there was no fluid in abdomen. There were increased bowel sounds on auscultation. On per rectal examination, a posterior mucosal tear of 3cms was noted. There was no active bleeding. There were no perianal bruises. Anal sphincter tone was normal. Bottom of a bottle was felt on rectal examination. Proctoscopy revealed bottom of a beer bottle.

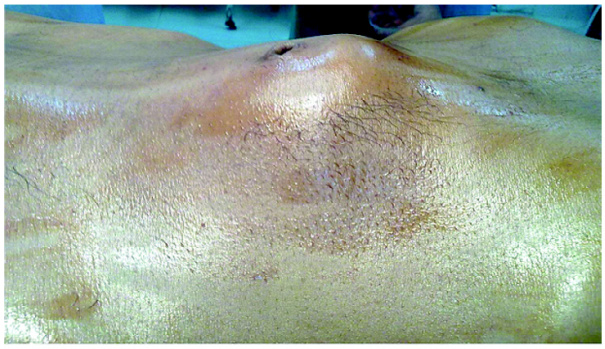

Fig.1: Photograph of abdomen showing an elevated, mass lesion of size 16X8 inches in the epigastric and umbilical regions

X-Ray abdomen revealed a radio opaque bottle in lower abdomen. (Fig 2).

CT abdomen confirmed the presence of beer bottle (fig,3). There was no evidence of pneumo-peritoneum or signs of peritonitis

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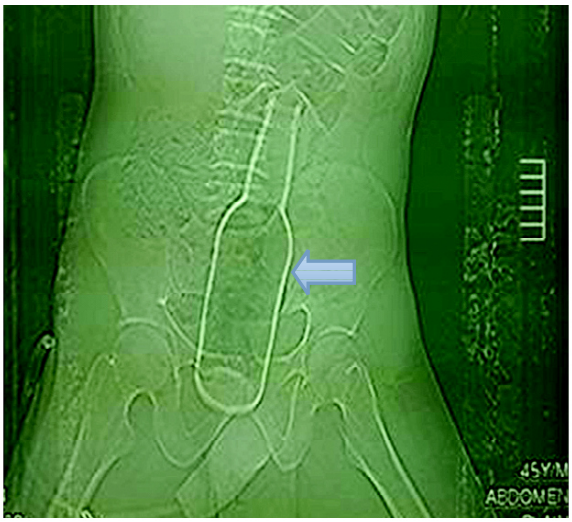

Fig 2 : Plain x-ray abdomen showing radio opaque shadow (blue arrow) of beer bottle which is placed vertically

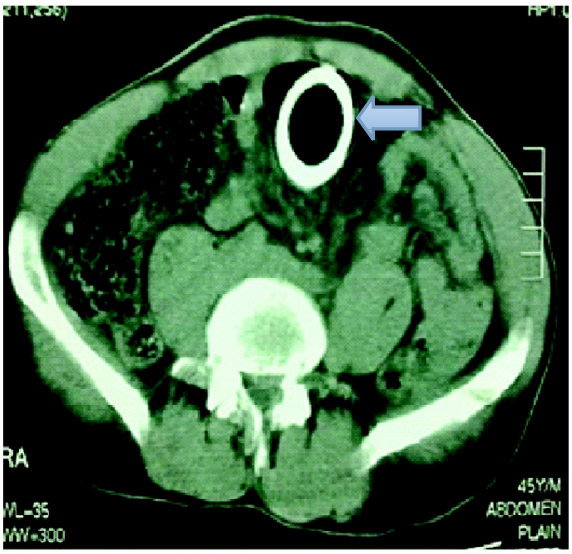

Fig 3 : C T scans of abdomen showing beer bottle (blue arrow). The glass rim with the hollow can be very clearly seen

Management

Bottle could not be delivered through rectum. Hence, Laparotomy under spinal Anaesthesia was performed through sub-umbilical midline linear incision .The beer bottle in sigmoid colon was removed without breaking it, by bimanual technique, pushing the beer bottle through the abdomen and pulling it through the anus (Figs.4,5,6)

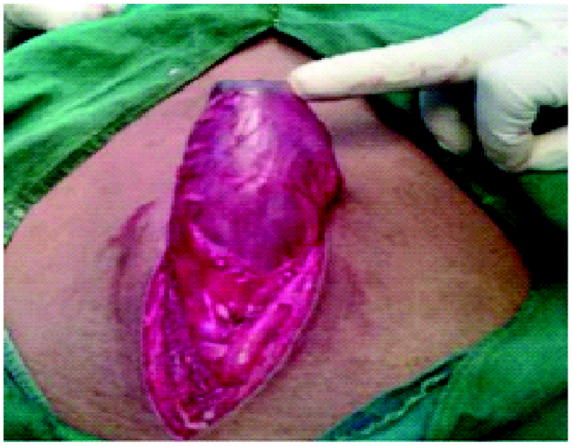

Fig 4 : Beer bottle in the recto-sigmoid through laparotomy incision

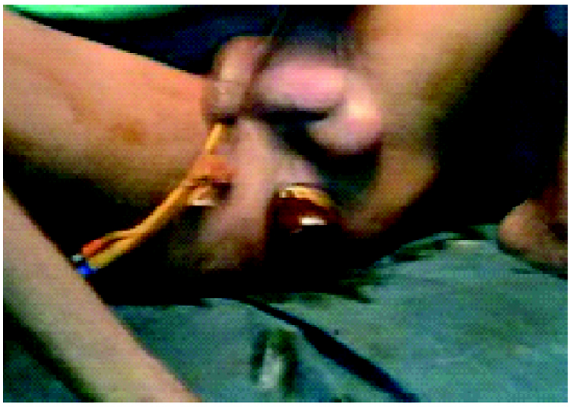

Fig 5 : Beer bottle being removed through the anus

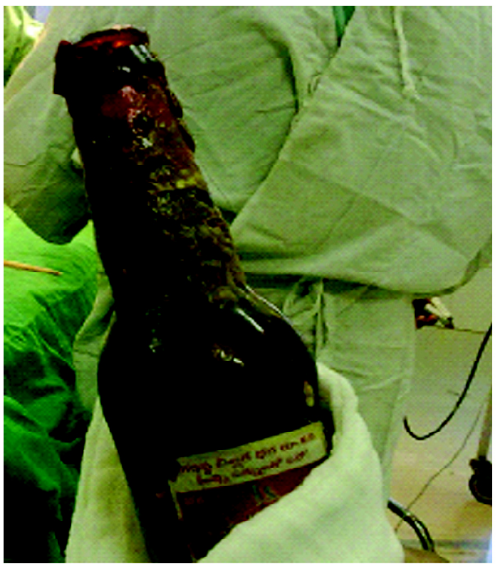

Fig 6 : Extracted beer bottle soiled with faecal matter

There was no evidence of peritonitis or free fluid. The post-operative period was uneventful. Abdominal sutures were removed on 9th post-operative day and patient was discharged. The post operative recovery was satisfactory during follow up of 2 years.

Discussion : The incidence of rectal foreign bodies varies according to region, uncommon in Asia and most common in Eastern Europe[8]. They can be seen in as young as 20s (mostly for eroticism) to as old as 60 s (mostly for the therapeutic purposes), with a mean age of 41 years. Anorectal foreign bodies are common in males than in females[9, 10].

Foreign Body in rectum can be classified as high lying or low- lying, depending on their location relative to the recto sigmoid junction. High lying objects cannot be removed through anorectum as they are not visualized, and unreachable. Low lying Foreign Bodies can be removed through anorectum as they are normally palpable. Removal is difficult if there is mucosal edema and muscular spasm which are due to delayed presentation. Rectal laceration and perforation may occur.

As per Barone et al assigned prognostic categories based on levels of injury.

Category I: Retained foreign body without injury.

Category II: Retained foreign body with mucosal laceration.

Category III: Retained foreign body with sphincter injury.

Category IV: Retained foreign body with rectal perforation.

The first step in evaluation and management of a patient with rectal body is to rule out rectal perforation and peritonitis by means of Physical examination, X-ray and CT Scan[9]. The plain radiography helps to localize the object and rule out free air.[11].

Conservative attempt is made to remove the object by means of digital manipulation if the object is visible[12]and patient is stable. Foreign bodies made of glass need special care to remove them intact. If end of the bottle is being grasped, pad the end of forceps to avoid breakage. The object may have to be redirected around the sacral curve for removal. If the suction created by the rectal mucosa is hindering removal, a Foley's catheter method of removal can be used. Some Foreign Bodies are removed successfully by uncommon method such as use of vacuum extraction device, plaster of Paris or obstetrics forceps. Once the object is removed, consider Sigmoidoscopy or Colonoscopy to detect possible mucosal injury.

If minimally invasive techniques fail, a definite procedure is chosen .Colonoscopy removal is also reported with good success[13]. Laparotomy is only required in impacted foreign body and or with perforation peritonitis. The laparoscopic approach is also a good treatment of choice for difficult cases as it allows for easy removal, detection of rectal injury, and early discharge[14]. Bak et al described a novel approach to retrieval and removal of a rectal FB utilizing a single-incision laparoscopic surgery port [15].

If perforation is present then primary repair, proximal loop colostomy, sigmoid end-colostomy and the Hartmann procedure, in combination with administration of wide spectrum antibiotics according to the severity of peritoneal contamination, can be performed. The mortality and morbidity rates of patients presenting with perforation above the peritoneal reflection of rectum have been reported to range from 2.5 to 20.0%[16] and 20.0 to 40.0%[17].

Conclusion

Rectal foreign bodies can present difficulty in diagnosis and management. ,so no single procedure is recommended. Thorough physical examination and radiography including CT are mandatory to localize the object, and know its size, so that a correct management can be planned. Care should be taken not to cause further damage while removing the foreign body.Laparotomy still has a place in removal of very large foreign bodies '.

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Case Report

Combined contribution of both anterior and posterior divisions of Internal Iliac artery

V Sunita

Abstract: Inferior gluteal, Internal pudendal and superior gluteal arteries are large caliber arteries of Internal iliac artery. "A unique variant contribution of both anterior and posterior divisions of Internal iliac artery in the formation of Inferior gluteal and Internal pudendal arteries" was found on the left side in a 55 year old male cadaver during regular dissection class of pelvic region for the first year medical undergraduates. To avoid accidental hemorrhage during pelvic surgeries and for interpretation of angiograms, it is necessary to have a sound knowledge of variations of Internal iliac artery and its branches for vascular surgeons and radiologists.

Key Words : Internal iliac artery, common trunk, anomalous

Introduction

Internal iliac artery one of the terminal branches of common iliac artery, extends from the lumbo-sacral intervertebral disc to the superior margin of greater sciatic foramen [1, 2]. During its course, it descends anterior to the sacro-iliac joint and divides into anterior & posterior divisions at the superior margin of greater sciatic notch. The Superior vesical, inferior vesical, middle rectal and obturator arteries arise from the anterior division, which terminates as Inferior gluteal and internal pudendal arteries [fig 1]. The inferior gluteal artery passes below the ventral ramus of the first sacral nerve, then between the piriformis and coccygeus and enter the gluteal region through the greater sciatic foramen. Internal pudendal artery provides blood to the external genitalia and is smaller in females than males. After its exit from the pelvis through the greater sciatic foramen, it crosses the dorsal surface of ischial spine and enters the perineum through the lesser sciatic foramen. Within the perineum, it traverses through the pudendal canal along with the internal pudendal veins and the pudendal nerve. The internal pudendal artery is sometimes smaller than usual, or fails to give off one or two of its usual branches; in such cases the deficiency is supplied by branches derived from an additional vessel, the accessory pudendal, which generally arises from the internal pudendal artery before its exit from the greater sciatic foramen. The Posterior division passes posterior to the greater sciatic foramen and gives off Ilio lumbar and lateral sacral arteries and continues as Superior gluteal artery. In the present case Ilio lumbar artery arose from the common trunk of Internal iliac artery and both inferior gluteal and internal pudendal arteries were formed by the contribution of both divisions of Internal iliac artery.

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Case report

The present case was a unilateral variant formation of the inferior gluteal and the internal pudendal arteries by the contribution of both the anterior and posterior divisions of the Internal iliac artery. This was found during the routine dissection class of pelvic region for the first year medical undergraduates in a 55 year old male cadaver. Ilio lumbar artery arose from the main trunk of left Internal iliac artery, which was 2.5 cm below the bifurcation of common iliac artery [Figure 1]. Lateral sacral artery, superior gluteal artery and the posterior root of the common trunk of the inferior gluteal and the internal pudendal artery originated from the posterior division of the internal iliac artery [fig 2]. Anterior root of the common trunk of inferior gluteal and internal pudendal artery originated from the anterior division and no variation found in the branches and their course [fig 2]. No variation found in the branches & their course of right internal iliac artery. Thus by both the roots the common trunk is formed, which runs downwards for 2.2cm over the piriformis muscle and then bifurcated into the Inferior gluteal artery and the Internal pudendal artery. The course of inferior gluteal and internal pudendal arteries was normal.

Discussion

The inferior gluteal, internal pudendal and superior gluteal arteries were categorized as large caliber vessels by Jastchinski in his study of polish subjects and he found that only the arteries of large caliber showed their regularity in their origin than medium and small caliber vessels, and classified the variations into four types[3]. Adachi modified the method by adding fifth variation by his study in Japanese subjects[4].

Type I- The superior gluteal artery arises separately from the Internal iliac artery, the inferior gluteal and internal pudendal arteries are given off by a common trunk. If the bifurcation occurs above the pelvic diaphragm it is considered as Type Ia, whereas if it occurs below pelvic diaphragm it is classified as Type Ib.

Type II- The superior and inferior gluteal arteries arise by a common trunk and internal pudendal artery separately.

Type III- The three branches arise separately from the internal iliac artery.

Type IV- The three branches arise by a common trunk.

Type V- The internal pudendal and the superior gluteal arteries arise from a common trunk and the inferior gluteal has a separate origin.

The present case is a rather rare variant of Type I a of Adachi's classification. In this type the Inferior gluteal and the Internal pudendal arteries arose by a common trunk and the Superior gluteal artery arose separately. Even though various workers reported the incidence of type I from 51.2% [4] to 60%[5], the present format of variation of the common trunk by the contribution from both the anterior and posterior divisions is not reported so far in the literature. The accidental hemorrhage is common during pelvic surgeries. Hemorrhage has been considered as the leading cause of maternal deaths in the developing countries[6]. The ligation of the internal iliac artery to control hemorrhage during pelvic surgeries has been described by Kelly HA as early as in 1894[7]. Recent reports opine that the efficacy of the internal iliac artery ligation during any obstetrics and gynecology surgery varies between 42 % to 75 %[8,9]. Knowledge of variations of Internal iliac artery and its branches is useful not only for anatomists, but also for pelvic suregeons during surgeries to prevent accidental hemorrhage and radiologists also for interpretation of angiograms.

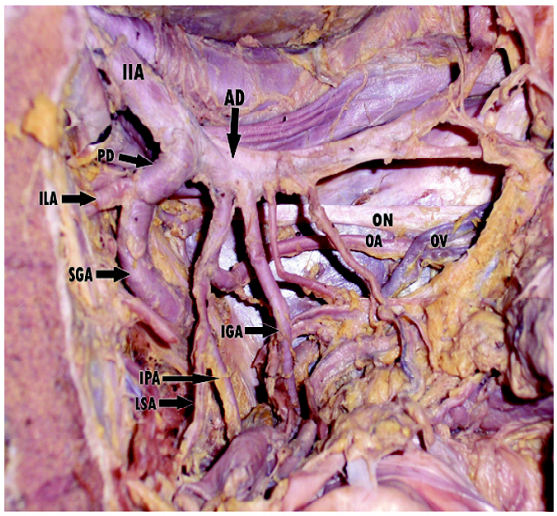

Figure 1: Showing normal course and branching pattern of Internal Iliac artery.

IIA: Internal iliac artery, ILA: Ilio lumbar artery, ON: Obturator nerve, OA; Obturator artery, AD; Anterior division of Internal iliac artery,PD: Posterior division of internal iliac artery, IVA: Inferior vesical artery, IGA: Inferior gluteal artery, IPA: Internal pudendal artery, SGA:Superior gluteal artery , OV: obturator vein.

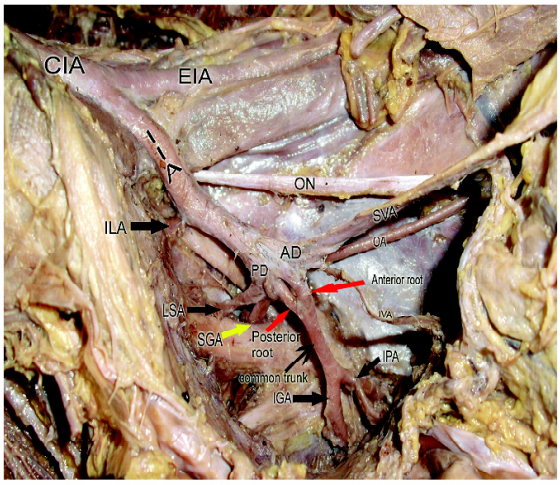

Figure 2: showing variant formation of common trunk of Inferior gluteal artery and Internal pudendal artery

CIA: Common iliac artery, EIA: External iliac artery, IIA: Internal iliac artery, ILA: Ilio lumbar artery, ON: Obturator nerve, OA; Obturator artery, AD; Anterior division of Internal iliac artery,PD: Posterior division of internal iliac artery, SVA: Superior vesical artery, IVA: Inferior vesical artery, IGA: Inferior gluteal artery, IPA: Internal pudendal artery, SGA; Superior gluteal artery

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